

# SUPPORTING INFORMATION

## The first Pd-catalyzed regioselective C-H functionalization of 2-pyrones

Michael J. Burns, Robert J. Thatcher, Richard J. K. Taylor\* and Ian J. S. Fairlamb\*

Department of Chemistry, University of York, Heslington, York, YO10 5DD, United Kingdom.

### TABLE OF CONTENTS

Title of section	Page
<b>1. General details</b>	<b>S2</b>
<b>2. Experimental procedures</b>	<b>S2</b>
Compound <b>1</b>	S3-S6
Compounds <b>5a-d</b>	S6-S9
Compounds <b>7a-l</b>	S9-S15
<b>3. Representative NMR Spectra for Compounds</b>	<b>S16</b>
Compound <b>4</b>	S16
Compounds <b>6a-d</b>	S17-S20
Compounds <b>8a-h</b>	S21-S29
Compound <b>10</b>	S29-S32
<b>4. X-ray Crystallography data for compounds</b>	<b>S33</b>
Table of all X-ray diffraction data	S34
Compound <b>6a</b>	S35
Compound <b>6b</b>	S35
Compound <b>8h</b>	S36
Compound <b>8i</b>	S36
Compound <b>10</b>	S37
Compound <b>12</b>	S38
<b>5. References</b>	<b>S39</b>

## 1. General Details

Reagents were purchased from either Sigma Aldrich or Alfa Aesar and used directly unless otherwise stated. Solvents were dried according to standard procedures prior to use and stored under nitrogen. Nitrogen gas was oxygen free and dried immediately before use via passage through sodium hydroxide pellets and silica. Argon and hydrogen were administered directly via balloon. The substructure 2*H*-pyran-2-one is henceforth referred to in the text as 2-pyrone.

4-Bromo-6-methyl-2-pyrone and 4-bromocoumarin were prepared using the procedure developed by Kato et al.<sup>1</sup> 4,6-Dichloro-2-pyrone and 4-chloro-2-pyrone were prepared according to the route used by Afarinkia et al.<sup>2</sup> Where commercially unavailable, 2-bromophenols were synthesised from the reaction of the corresponding phenol with Br<sub>2</sub>.<sup>3</sup> 4-Hydroxy-6-phenethyl-2-pyrone was synthesised according to the procedure developed by Zhang et al.<sup>4</sup>

All TLC analysis was performed using Merck 5554 aluminium backed silica plates and visualised using UV light (254 nm), an aqueous solution of potassium permanganate, or an ethanol based solution of *p*-anisaldehyde. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Jeol ECX400 spectrometer operating at 400 and 100 MHz respectively, or a Bruker 500 spectrometer operating at 500 and 126 MHz respectively. All column chromatography was performed using flash silica-gel with the solvent systems specified within the text.

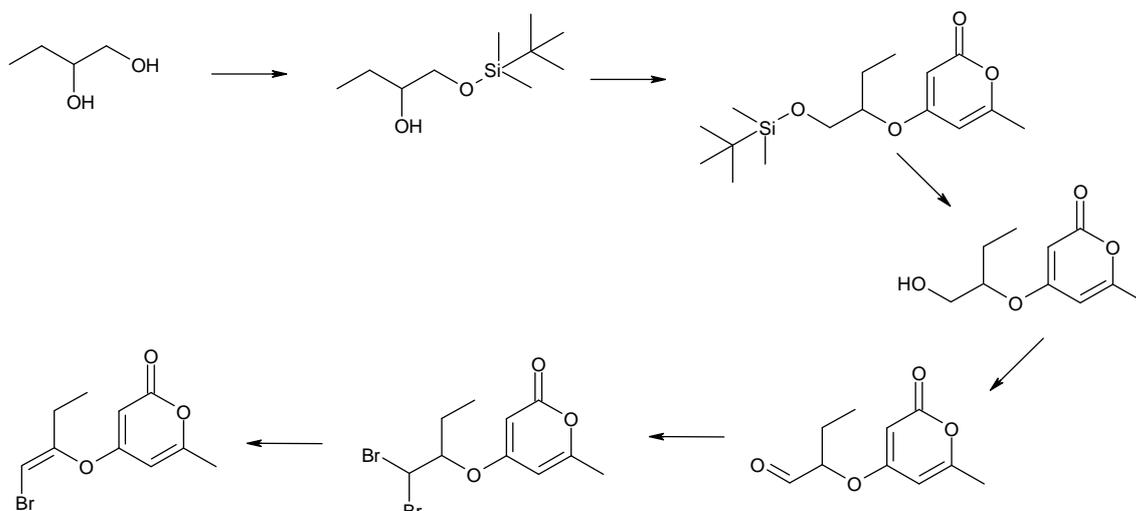
## 2. Experimental Procedures

### General Procedure A - Synthesis of 4-(2-haloaryloxy)-2-pyrones

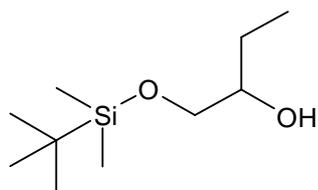
A solution of 4-Bromo-6-methyl-2-pyrone (1 eq.), 2-halophenol (1.1 eq.), and K<sub>2</sub>CO<sub>3</sub> (1.5 eq.) in acetone (4 mL/mmol) was stirred at 60 °C for 16 hours. The reaction was quenched by addition of water and ethyl acetate, and the layers separated. The aqueous layer was extracted 3 times using ethyl acetate and the combined organic extracts dried over MgSO<sub>4</sub>, filtered and concentrated *in vacuo* and purified by flash column chromatography (10-30 % EtOAc in hexanes).

## Synthesis of 4-[[*Z*]-2-Bromo-1-ethyl-1-ethenyl]oxy}-6-methyl-2-pyrone (1)

Note that compound needed to be prepared by a six step procedure. All preparative and characterization details are therefore included here (a general scheme is given below).



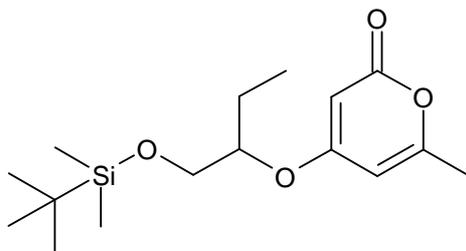
### 1-(*tert*-Butyl-dimethyl-silyloxy)-butan-2-ol



A solution of butane-1,2-diol (20 mmol, 1 eq.), TEA (40 mmol, 2 eq.) and *tert*-butyl-dimethylsilyl chloride (30 mmol, 1.5 eq.) under nitrogen in DCM (25 mL), was stirred at 20 °C for 16 h. The reaction was then quenched with ice cold water (15 mL) and the aqueous layer removed. The organic layer was then washed with brine (15 mL) and dried over MgSO<sub>4</sub> then concentrated *in vacuo* to afford the crude material. The product was purified via distillation (70 °C, 0.7 mbar) to afford a colourless oil (3.43 g, 84.1%).

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 3.63 (dd, *J* = 9.7, 3.3 Hz, 1H), 3.55 (ddt, *J* = 10.5, 7.2, 3.3 Hz, 1H), 3.39 (dd, *J* = 9.7, 7.2 Hz, 1H), 1.40-1.48 (m, 2H), 0.95 (t, *J* = 7.5 Hz, 3H), 0.89 (s, 9H), 0.07 (s, 6H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 73.3, 67.0, 26.0, 21.7, 18.4, 10.0, -5.3, -5.3; MS (ESI) *m/z* (rel.%): 205 [MH<sup>+</sup>] (100); IR (neat): 3406, 2955, 2929, 2858, 1462, 1253, 1092, 834, 774 cm<sup>-1</sup>.

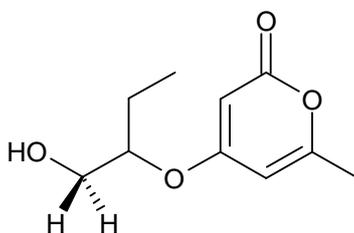
#### 4-[1-(*tert*-Butyl-dimethyl-silyloxymethyl)-propoxy]-6-methyl-2-pyrone



4-hydroxy-6-methyl-2-pyrone (4 mmol, 1eq.), alcohol 1-(*tert*-Butyl-dimethyl-silyloxy)-butan-2-ol (6 mmol, 1.5 eq.) and triphenylphosphine (6 mmol, 1.5 eq.) were dissolved in THF (8 mL) under nitrogen at 0 °C. DIAD (6 mmol, 1.5 eq.) was then added carefully over 15. The reaction was stirred for 16h at 20 °C and then the solvent removed *in vacuo*. The crude product was purified *via* column chromatography (20% EtOAc in hexanes) to afford a colourless oil (1.23 g, 98.4%).

R<sub>f</sub> = 0.56 (20% EtOAc in hexanes); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 5.71 (dq, *J* = 1.9, 0.8 Hz, 1H, C<sup>5</sup>H), 5.36 (d, *J* = 1.9 Hz, 1H), 4.17 (p, *J* = 5.4 Hz, 1H), 3.66 (s, 1H), 3.64 (d, *J* = 1.3 Hz, 1H), 2.11-2.15 (m, 3H), 1.53-1.69 (m, 2H), 0.87 (t, *J* = 7.5 Hz, 3H), 0.79 (s, 9H), -0.03 (s, 3H), -0.04 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 170.5, 165.3, 162.1, 100.9, 88.4, 80.9, 63.8, 25.8, 23.4, 19.8, 18.2, 9.5, -5.4, -5.4; MS (ESI) *m/z* (rel.%): 335 [MNa<sup>+</sup>] (100), 313 [MH<sup>+</sup>] (2); HRMS (ESI) calculated for C<sub>16</sub>H<sub>28</sub>O<sub>4</sub>NaSi [M<sup>+</sup>]: 335.1649, found: 335.1640; IR (neat): 2929, 2883, 2857, 1736, 1651, 1563, 1450, 1414, 1320, 1249, 1139, 1036, 1001 cm<sup>-1</sup>.

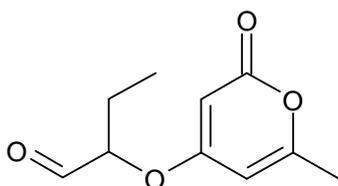
#### 4-(1-Hydroxymethyl-propoxy)-6-methyl-2-pyrone



A solution of 4-[1-(*tert*-Butyl-dimethyl-silyloxymethyl)-propoxy]-6-methyl-2-pyrone (3 mmol, 1eq.) in THF (15 mL), water (7.5 mL) and acetic acid (25 mL) was stirred for 16 hours at 20 °C. The solution was concentrated *in vacuo* and the resulting product was purified by column chromatography (2-4% MeOH in DCM) to afford a pale yellow oil (582 mg, 98%).

R<sub>f</sub> = 0.21 (5% MeOH in DCM); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 5.80 (dq, *J* = 2.2, 0.8 Hz, 1H), 5.46 (d, *J* = 2.2 Hz, 1H), 4.28 (qd, *J* = 5.9, 4.1 Hz, 1H), 3.81 (dd, *J* = 12.1, 4.1 Hz, 1H), 3.68 (dd, *J* = 12.1, 5.9 Hz, 1H), 2.18 (q, *J* = 0.8 Hz, 3H), 2.07 (s, 1H), 1.66-1.74 (m, 2H), 0.93 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) 170.5, 165.6, 162.5, 101.2, 88.7, 81.2, 63.4, 23.2, 20.0, 9.6; MS (ESI) *m/z* (rel.%): 221 [MNa<sup>+</sup>] (100), 199 [MH<sup>+</sup>] (6); HRMS (ESI) calculated for C<sub>10</sub>H<sub>14</sub>O<sub>4</sub>Na [M<sup>+</sup>]: 221.0784, found: 221.0790; IR (neat): 3411, 2971, 2939, 1687, 1644, 1556, 1449, 1415, 1246, 1148, 1058, 1039, 1001, 877, 818, 750 cm<sup>-1</sup>.

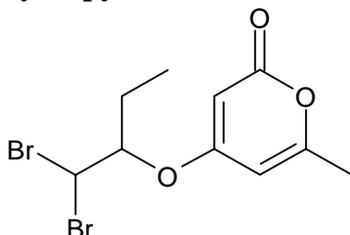
## 2-(6-Methyl-2-pyrone-4-yloxy)-butyraldehyde



To a solution of oxalyl chloride (0.83 g, 6.5 mmol, 1.3 eq.) in DCM (15 mL) at  $-78\text{ }^{\circ}\text{C}$ , was added DMSO (1.01 g, 13 mmol, 2.6 eq.) in DCM (15 mL) dropwise over 15 minutes. The solution was stirred for 30 minutes at  $-78\text{ }^{\circ}\text{C}$  then a solution of 4-(1-Hydroxymethyl-propoxy)-6-methyl-2-pyrone (0.99 g, 5 mmol, 1 eq.) in DCM (15 mL) was added dropwise over 20 minutes. The solution was stirred for 30 minutes at  $-78\text{ }^{\circ}\text{C}$  then  $\text{Et}_3\text{N}$  (1.8g, 18 mmol, 3.6 eq.) added dropwise over 15 minutes and the reaction stirred for a further 60 minutes at  $-78\text{ }^{\circ}\text{C}$  then allowed to warm slowly to ambient temperature. The solvent was removed in *vacuo*, and the crude residue taken up in  $\text{Et}_2\text{O}$  and passed through a silica plug, eluting with  $\text{Et}_2\text{O}$ . Concentration of the eluent afforded the title compound as a white solid used without further purification (913 mg, 93%).

$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 9.57 (d,  $J = 1.2\text{ Hz}$ , 1H), 5.88 (d,  $J = 2.1\text{ Hz}$ , 1H), 5.23 (d,  $J = 2.1\text{ Hz}$ , 1H), 4.47 (ddd,  $J = 7.0, 5.4, 1.2\text{ Hz}$ , 1H), 2.22 (s, 3H), 1.85-2.00 (m, 2H), 1.03 (t,  $J = 7.4\text{ Hz}$ , 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 198.4, 169.4, 164.4, 163.0, 100.3, 89.1, 82.9, 23.0, 20.0, 9.1; **IR** (DCM): 3608, 3376, 3061, 2965, 1710, 1650, 1566, 1450, 1413, 1322, 1244, 1146, 1093  $\text{cm}^{-1}$ .

## 4-[1-(Dibromomethyl)propoxy]-6-methyl-2-pyrone

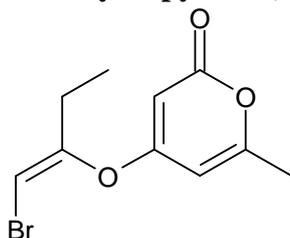


Following the known procedure:<sup>5</sup> To a solution of triphenyl phosphite (748 mg, 2.4 mmol, 1.1 eq.) in DCM (10 mL) under argon at  $-60\text{ }^{\circ}\text{C}$ , was added  $\text{Br}_2$  (405 mg, 2.53 mmol, 1.15 eq.) dropwise over 10 minutes, followed by  $\text{Et}_3\text{N}$  (267 mg, 2.64 mmol, 1.2 eq.) and 2-(6-Methyl-2-pyrone-4-yloxy)-butyraldehyde (430 mg, 2.2 mmol, 1 eq.). The reaction was allowed to warm slowly to ambient temperature whilst stirring for 18 hours, followed by a further 2 hours heating to reflux. Removal of solvent in *vacuo* followed by flash column chromatography (20%  $\text{EtOAc}$  in hexanes) afforded the title compound as a white powder (265 mg, 36%).

$R_f = 0.22$  (20%  $\text{EtOAc}$  in hexanes);  $^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ ): 5.86 (dq,  $J = 2.3, 0.8\text{ Hz}$ , 1H,  $\text{C}^5\text{H}$ ), 5.83 (d,  $J = 4.1\text{ Hz}$ , 1H,  $\text{C}^{10}\text{H}$ ), 5.43 (d,  $J = 2.3$ , 1H,  $\text{C}^3\text{H}$ ), 4.45 (td,  $J = 8.0, 4.1\text{ Hz}$ , 1H,  $\text{C}^{11}\text{H}$ ), 2.22 (app. s, 3H,  $\text{C}^7\text{H}_3$ ), 2.07 – 1.86 (m, 2H,  $\text{C}^9\text{H}_2$ ), 1.01 (t,  $J = 7.5\text{ Hz}$ , 3H,  $\text{C}^8\text{H}_3$ );  $^{13}\text{C-NMR}$  (126 MHz,  $\text{CDCl}_3$ ): 169.5, 164.5, 163.0, 100.4, 88.8, 82.4, 71.2, 22.9, 19.9, 9.3; **MS** (ESI)  $m/z$  (rel.%): 343 [ $^{81}\text{Br}/^{81}\text{Br} - \text{MH}^+$ ] (44), 341 [ $^{79}\text{Br}/^{81}\text{Br} - \text{MH}^+$ ] (100), 339 [ $^{79}\text{Br}/^{79}\text{Br} - \text{MH}^+$ ] (45); **HRMS** (ESI) calculated for  $\text{C}_{10}\text{H}_{13}\text{Br}_2\text{O}_3$ : 338.9226,

found: 338.9223; **IR** (neat): 3078, 3017, 2975, 2943, 2159, 1702, 1646, 1558, 1443, 1409, 1248, 1230, 1146, 996, 867, 829, 810, 673  $\text{cm}^{-1}$ .

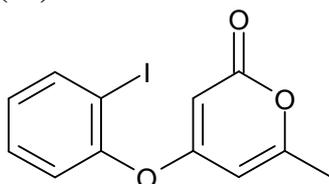
#### 4-[(Z)-2-Bromo-1-ethyl-1-ethenyl]oxy-6-methyl-2-pyrone (1)



To a solution of 4-[1-(Dibromomethyl)propoxy]-6-methyl-2-pyrone (340 mg, 1 mmol, 1 eq.) in THF (3 mL) under nitrogen, was added DBU (304 mg, 2 mmol, 2 eq.) and the solution stirred for 24 hours at 70 °C. The reaction was allowed to cool and quenched by the addition of water (1 mL). The solution was then extracted by EtOAc (3 × 3 mL) and the combined organic extracts dried over  $\text{MgSO}_4$  and concentrated in *vacuo* to afford the crude product. Purification by flash column chromatography (15% EtOAc in hexanes) afforded the title compound as pale yellow oil (167 mg, 64.5%).

R<sub>f</sub> = 0.26 (20% EtOAc in hexanes); **<sup>1</sup>H-NMR** (500 MHz,  $\text{CDCl}_3$ ): 5.95 (t,  $J$  = 1.3 Hz, 1H,  $\text{C}^{11}\text{H}$ ), 5.92 (dq,  $J$  = 2.2, 0.8 Hz, 1H,  $\text{C}^5\text{H}$ ), 5.40 (dq,  $J$  = 2.2, 0.5 Hz, 1H,  $\text{C}^3\text{H}$ ), 2.29 (qd,  $J$  = 7.5, 1.3 Hz, 2H,  $\text{C}^9\text{H}_2$ ), 2.25 (dd,  $J$  = 0.8, 0.5 Hz, 3H,  $\text{C}^7\text{H}_3$ ), 1.11 (t,  $J$  = 7.5 Hz, 3H,  $\text{C}^8\text{H}_3$ ); **<sup>13</sup>C-NMR** (126 MHz,  $\text{CDCl}_3$ ): 169.0, 164.3, 163.5, 155.0, 99.5, 97.9, 91.0, 23.3, 20.0, 10.4; **MS** (ESI)  $m/z$  (rel.%): 283 [ $^{81}\text{Br-MNa}^+$ ] (42), 281 [ $^{79}\text{Br-MNa}^+$ ] (42), 261 [ $^{81}\text{Br-MH}^+$ ] (98), 259 [ $^{79}\text{Br-MH}^+$ ] (100); **HRMS** (ESI) calculated for  $\text{C}_{10}\text{H}_{12}\text{BrO}_3$ : 258.9964, found: 258.9964; **IR** (neat): 3089, 2975, 2938, 1711, 1642, 1565, 1446, 1405, 1220, 1174, 1138, 998, 849, 819  $\text{cm}^{-1}$ .

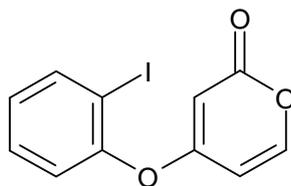
#### 4-(2-Iodophenoxy)-6-methyl-2-pyrone (5a)



The title compound was prepared according to General Procedure A, on a 10 mmol scale, to afford the product as a white solid (2.77g, 84.5%).

Mpt: 71-73 °C; **<sup>1</sup>H-NMR** (400 MHz,  $\text{CDCl}_3$ ): 7.86 (dd,  $J$  = 7.9, 1.5 Hz, 1H), 7.40 (td,  $J$  = 7.9, 1.5 Hz, 1H), 7.09 (dd,  $J$  = 7.9, 1.5 Hz, 1H), 7.03 (td,  $J$  = 7.9, 1.5 Hz, 1H), 6.02 (dq,  $J$  = 2.3, 1.0 Hz,  $\text{C}^5\text{H}$ , 1H), 5.05 (d,  $J$  = 2.3,  $\text{C}^3\text{H}$ , 1H), 2.26 (d,  $J$  = 1.0 Hz,  $\text{C}^7\text{H}_3$ , 3H); **<sup>13</sup>C-NMR** (101 MHz,  $\text{CDCl}_3$ ): 169.5, 164.3, 163.6, 152.2, 140.3, 130.1, 128.3, 122.3, 99.7, 91.2, 89.6, 20.1; **MS** (ESI)  $m/z$  (rel.%): 351 [ $\text{MNa}^+$ ] (100), 329 [ $\text{MH}^+$ ] (97); **HRMS** (ESI) calculated for  $\text{C}_{12}\text{H}_9\text{INaO}_3$ : 350.9489, found: 350.9484; **IR** (neat): 3806, 1697, 1636, 1559, 1437, 1398, 1223, 820, 764  $\text{cm}^{-1}$ .

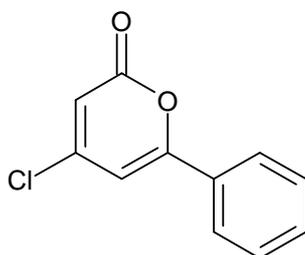
#### 4-(2-Iodophenoxy)-2-pyrone (5b)



A solution of 4-chloro-2-pyrone (125 mg, 0.96 mmol, 1 eq.), 2-iodophenol (253 mg, 1.15 mmol, 1.2 eq.), and  $K_2CO_3$  (264 mg, 1.9 mmol, 2 eq.) in acetone (5 mL) was stirred at 60 °C for 16 hours. The reaction was quenched by addition of water (2 mL) and ethyl acetate (5 mL), and the layers separated. The aqueous layer was extracted using ethyl acetate (3 × 5 mL) and the combined organic extracts dried over  $MgSO_4$ , filtered and concentrated *in vacuo*. Purification by flash column chromatography (20% EtOAc in hexanes) afforded the title compound as a white solid (260.2 mg, 86.5%).

Mpt: 92-93 °C;  $^1H$ -NMR (400 MHz,  $CDCl_3$ ): 7.89 (dd,  $J = 7.9, 1.5$  Hz, 1H), 7.50 (dd,  $J = 5.8, 0.7$  Hz, 1H), 7.42 (ddd,  $J = 8.1, 7.5, 1.5$  Hz, 1H), 7.12 (dd,  $J = 8.1, 1.5$  Hz, 1H), 7.05 (ddd,  $J = 7.9, 7.5, 1.5$  Hz, 1H), 6.27 (dd,  $J = 5.8, 2.4$  Hz, 1H), 5.20 (dd,  $J = 2.4, 0.7$  Hz, 1H);  $^{13}C$ -NMR (101 MHz,  $CDCl_3$ ): 168.4, 163.5, 152.5, 152.1, 140.4, 130.2, 128.4, 122.3, 102.8, 94.2, 89.5; MS (ESI)  $m/z$  (rel.%): 337 [ $MNa^+$ ] (15), 315 [ $MH^+$ ] (100); HRMS (ESI) calculated for  $C_{11}H_8IO_3$ : 314.9513, found: 314.9516; IR (neat): 3087, 1700, 1633, 1556, 1434, 1328, 1218, 1195, 1158, 1054, 881, 821, 770  $cm^{-1}$ .

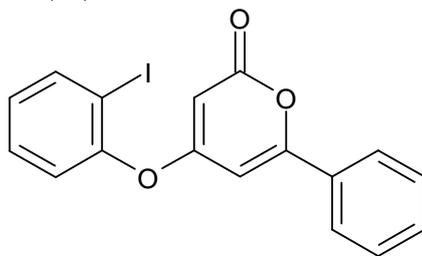
#### 4-Chloro-6-phenyl-2-pyrone



To a solution of 4,6-dichloro-2-pyrone (330 mg, 2 mmol, 1 eq.) and  $NiCl_2(PPh_3)_2$  (21.7 mg, 0.04 mmol, 2 mol%) in THF (4 mL) under nitrogen at 20 °C, was added 2.0 M PhMgBr in THF (1 mL, 2 mmol, 1 eq.). The reaction was then stirred at 20 °C for 24 hours then quenched by the addition of water (2 mL) and EtOAc (5 mL). The organic layer was separated and the aqueous layer extracted with EtOAc (2 × 5 mL). The combined organic extracts were concentrated *in vacuo* and purified by flash column chromatography (10% EtOAc in hexanes) to afford a white crystalline solid (62.7 mg, 15.2%).

Mpt: 103-105 °C;  $^1H$ -NMR (400 MHz,  $CDCl_3$ ): 7.79 – 7.86 (m, 2H), 7.44 – 7.54 (m, 3H), 6.70 (d,  $J = 1.7$  Hz, 1H), 6.35 (d,  $J = 1.7$  Hz, 1H);  $^{13}C$ -NMR (101 MHz,  $CDCl_3$ ): 160.6, 160.5, 151.9, 131.7, 130.2, 129.1, 125.9, 111.8, 103.6; MS (ESI)  $m/z$  (rel.%): 231 [ $^{37}Cl-MNa^+$ ] (14), 229 [ $^{35}Cl-MNa^+$ ] (49), 209 [ $^{37}Cl-MH^+$ ] (31), 207 [ $^{35}Cl-MH^+$ ] (100); HRMS (ESI) calculated for  $C_{11}H_8ClO_2$ : 207.0207, found: 207.0209; IR (neat): 3079, 1721, 1706, 1612, 1537, 1494, 1451, 1364, 1328, 1235, 1149, 1088, 1050, 859, 813, 776  $cm^{-1}$ .

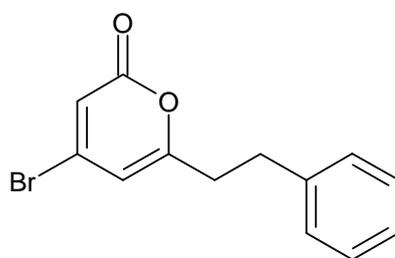
#### 4-(2-Iodophenoxy)-6-phenyl-2-pyrone (5c)



A solution of 4-Chloro-6-phenyl-2-pyrone (50.0 mg, 0.24 mmol, 1 eq.), 2-iodophenol (64 mg, 0.29 mmol, 1.2 eq.), and  $K_2CO_3$  (50 mg, 0.36 mmol, 1.5 eq.) in acetone (1 mL) was stirred at 60 °C for 16 hours. The reaction was quenched by addition of water (1 mL) and ethyl acetate (3 mL), and the layers separated. The aqueous layer was extracted using ethyl acetate (3 × 3 mL) and the combined organic extracts dried over  $MgSO_4$ , filtered and concentrated *in vacuo*. Purification by flash column chromatography (20% EtOAc in hexanes) afforded the title compound as a white solid (77.6 mg, 82.9%).

Mpt: 155-157 °C;  $^1H$ -NMR (400 MHz,  $CDCl_3$ ): 7.91 (dd,  $J = 8.0, 1.5$  Hz, 1H), 7.84 – 7.89 (m, 2H), 7.47 – 7.52 (m, 3H), 7.44 (ddd,  $J = 8.1, 7.4, 1.5$  Hz, 1H), 7.17 (dd,  $J = 8.1, 1.5$  Hz, 1H), 7.07 (ddd,  $J = 8.0, 7.4, 1.5$  Hz, 1H), 6.70 (d,  $J = 2.1$  Hz, 1H), 5.20 (d,  $J = 2.1$  Hz, 1H);  $^{13}C$ -NMR (101 MHz,  $CDCl_3$ ): 169.6, 163.7, 161.5, 152.4, 140.4, 131.3, 130.9, 130.2, 128.0, 128.4, 125.8, 122.4, 97.3, 92.2, 89.7; MS (ESI)  $m/z$  (rel.%): 413 [ $MNa^+$ ] (34), 391 [ $MH^+$ ] (100); HRMS (ESI) calculated for  $C_{17}H_{12}IO_3$ : 390.9826, found: 390.9820; IR (neat): 3093, 2962, 1698, 1629, 1555, 1402, 1257, 1218, 1173, 1020, 808, 766  $cm^{-1}$ .

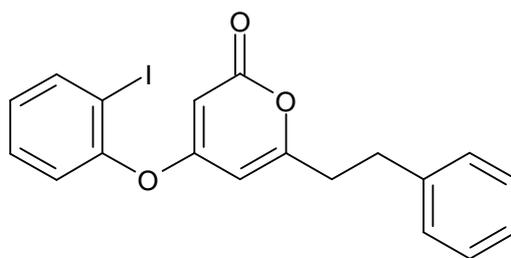
#### 4-Bromo-6-phenethyl-2-pyrone



To a solution of 4-hydroxy-6-phenethyl-2-pyrone (100 mg, 0.46 mmol, 1 eq.) in DMF (1 mL) under nitrogen, was added dropwise  $PBr_3$  (502 mg, 1.85 mmol, 4 eq.) over 10 minutes. The reaction was then stirred at 80 °C for 18 hours and allowed to cool to ambient temperature, then DMF was removed under high vacuum and water (2 mL) and  $Et_2O$  (5 mL) added. The organic layer was separated and the aqueous layer extracted with  $Et_2O$  (5 × 5 mL) then the combined organic extracts dried over  $MgSO_4$  and concentrated *in vacuo* to give the crude product. Purification via flash column chromatography (10% EtOAc in hexanes) gave the title compound as a yellow oil. (50.3 mg, 39.2%).

$^1H$ -NMR (400 MHz,  $CDCl_3$ ): 7.20 – 7.26 (m, 2H), 7.17 (m, 1H), 7.07 – 7.11 (m, 2H), 6.39 (d,  $J = 1.6$  Hz, 1H), 6.05 (d,  $J = 1.6$  Hz, 1H), 2.90 (t,  $J = 7.9$  Hz, 2H), 2.70 (t,  $J = 7.9$  Hz, 2H);  $^{13}C$ -NMR (101 MHz,  $CDCl_3$ ): 164.3, 160.6, 141.0, 139.4, 128.6, 128.2, 126.6, 115.1, 108.2, 35.4, 32.8; MS (ESI)  $m/z$  (rel.%): 303 [ $^{81}Br-MNa^+$ ] (57), 301 [ $^{79}Br-MNa^+$ ] (58), 281 [ $^{81}Br-MH^+$ ] (96), 279 [ $^{79}Br-MH^+$ ] (100); HRMS (ESI) calculated for  $C_{13}H_{12}BrO_2$ : 279.0015, found: 279.0010;

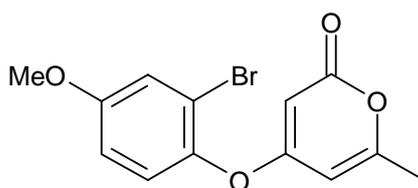
#### 4-(2-Iodophenoxy)-6-phenethyl-2-pyrone (5d)



A solution of 4-Bromo-6-phenethyl-2-pyrone (45.0 mg, 0.16 mmol, 1 eq.), 2-iodophenol (40 mg, 0.18 mmol, 1.1 eq.), and  $K_2CO_3$  (33 mg, 0.24 mmol, 1.5 eq.) in acetone (1 mL) was stirred at 60 °C for 16 hours. The reaction was quenched by addition of water (1 mL) and ethyl acetate (3 mL), and the layers separated. The aqueous layer was extracted using ethyl acetate (3 × 3 mL) and the combined organic extracts dried over  $MgSO_4$ , filtered and concentrated *in vacuo*. Purification by flash column chromatography (20% EtOAc in hexanes) afforded the product as a yellow solid (39.4 mg, 58.9%).

$^1H$ -NMR (400 MHz,  $CDCl_3$ ): 7.87 (dd,  $J = 7.9, 1.5$  Hz, 1H), 7.40 (ddd,  $J = 8.1, 7.4, 1.5$  Hz, 1H), 7.27–7.34 (m, 2H), 7.23 (m, 1H), 7.17–7.21 (m, 2H), 7.08 (dd,  $J = 8.1, 1.5$  Hz, 1H), 7.04 (td,  $J = 1.5, 7.8$ , 1H), 5.95 (d,  $J = 2.2$  Hz, 1H), 5.08 (d,  $J = 2.2$  Hz, 1H), 2.98–3.06 (m, 2H), 2.79–2.88 (m, 2H);  $^{13}C$ -NMR (101 MHz,  $CDCl_3$ ): 169.3, 165.9, 164.3, 152.3, 140.3, 139.7, 130.1, 128.6, 128.3, 128.3, 126.5, 122.3, 99.7, 91.6, 89.6, 35.7, 32.9; MS (ESI)  $m/z$  (rel.%): 441 [ $MNa^+$ ] (16), 419 [ $MH^+$ ] (100); HRMS (ESI) calculated for  $C_{19}H_{16}IO_3$ : 419.0139, found: 419.0130; IR (DCM): 3065, 3030, 2932, 1724, 1643, 1571, 1497, 1329, 1269, 1262, 1227, 1131, 1022  $cm^{-1}$ .

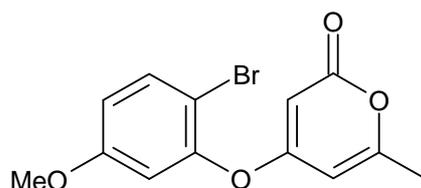
#### 4-(2-Bromo-4-methoxy-phenoxy)-6-methyl-2-pyrone (7a)



The title compound was prepared according to General Procedure A, on a 1 mmol scale, to afford the product as a white solid (279.3 mg, 89.8%).

Mpt: 98–99 °C;  $^1H$ -NMR (400 MHz,  $CDCl_3$ ): 7.15 (d,  $J = 2.9$  Hz, 1H), 7.04 (d,  $J = 8.9$  Hz, 1H), 6.88 (dd,  $J = 8.9, 2.9$  Hz, 1H), 6.00 (d,  $J = 2.2$  Hz, 1H), 5.08 (d,  $J = 2.2$  Hz, 1H), 3.81 (s, 3H), 2.26 (s, 3H);  $^{13}C$ -NMR (101 MHz,  $CDCl_3$ ): 170.1, 164.5, 163.4, 158.2, 142.9, 123.3, 118.8, 116.1, 114.8, 99.5, 90.8, 55.9, 20.0; MS (ESI)  $m/z$  (rel.%): 335 [ $^{81}Br$ - $MNa^+$ ] (99), 333 [ $^{79}Br$ - $MNa^+$ ] (100), 313 [ $^{81}Br$ - $MH^+$ ] (93), 311 [ $^{79}Br$ - $MH^+$ ] (311); HRMS (ESI) calculated for  $C_{13}H_{12}BrO_4$  [ $MH^+$ ]: 310.9913, found: 310.9909; IR (neat): 3193, 3087, 1726, 1647, 1569, 1491, 1446, 1403, 1211, 1133, 1018, 982, 841, 805, 779  $cm^{-1}$ .

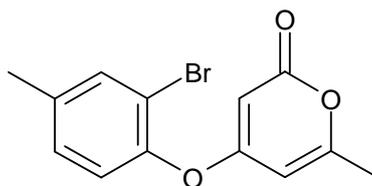
#### 4-(2-Bromo-5-methoxy-phenoxy)-6-methyl-2-pyrone (7b)



The title compound was prepared according to General Procedure A, on a 3 mmol scale, to afford the product as a white solid (492 mg, 52.7%).

Mpt: 103-106 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.15 (d, *J* = 2.9 Hz, 1H), 7.04 (d, *J* = 8.9 Hz, 1H), 6.88 (dd, *J* = 8.9, 2.9 Hz, 1H), 6.00 (d, *J* = 2.2 Hz, 1H), 5.08 (d, *J* = 2.2 Hz, 1H), 3.81 (s, 3H), 2.26 (s, 3H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 170.1, 164.5, 163.4, 158.2, 142.9, 123.3, 118.8, 116.1, 114.8, 99.5, 90.8, 55.9, 20.0; MS (ESI) *m/z* (rel.%): 335 [<sup>81</sup>Br-MNa<sup>+</sup>] (68), 333 [<sup>79</sup>Br-MNa<sup>+</sup>] (70), 313 [<sup>81</sup>Br-MH<sup>+</sup>] (100), 311 [<sup>79</sup>Br-MH<sup>+</sup>] (100); HRMS (ESI) calculated for C<sub>13</sub>H<sub>12</sub>BrO<sub>4</sub> [MH<sup>+</sup>]: 310.9913, found: 310.9909; IR (neat): 3066, 1709, 1645, 1566, 1483, 1441, 1399, 1314, 1236, 1199, 1137, 1018, 991, 858, 836 cm<sup>-1</sup>.

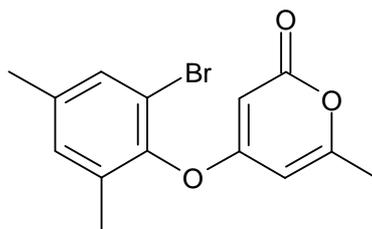
#### 4-(2-Bromo-4-methylphenoxy)-6-methyl-2-pyrone (7c)



The title compound was prepared according to General Procedure A, on a 1 mmol scale, to afford the product as a white solid (283.5 mg, 96.1%).

Mpt: 64-65 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.46 (d, *J* = 1.5 Hz, 1H), 7.15 (dd, *J* = 1.5, 8.1 Hz, 1H), 7.00 (d, *J* = 8.1 Hz, 1H), 6.00 (dq, *J* = 2.2, 0.9 Hz, 1H), 5.08 (d, *J* = 2.2, 1H), 2.36 (s, 3H), 2.26 (d, *J* = 0.9 Hz, 3H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 169.8, 164.4, 163.5, 147.0, 138.3, 134.4, 129.7, 122.6, 115.4, 99.6, 90.9, 20.6, 20.0; MS (ESI) *m/z* (rel.%): 297 [<sup>81</sup>Br-MH<sup>+</sup>] (98), 295 [<sup>79</sup>Br-MH<sup>+</sup>] (100); HRMS (ESI) calculated for C<sub>13</sub>H<sub>12</sub>BrO<sub>3</sub> [<sup>79</sup>Br-MH<sup>+</sup>]: 294.9964, found: 294.9972; IR (neat): 3072, 1726, 1648, 1561, 1488, 1449, 1395, 1316, 1239, 1128, 850, 830 cm<sup>-1</sup>.

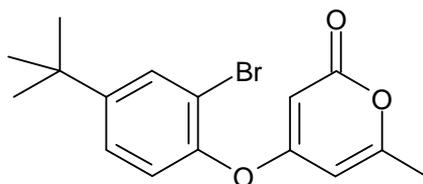
#### 4-(2-Bromo-4,6-dimethyl-phenoxy)-6-methyl-2-pyrone (7d)



The title compound was prepared according to General Procedure A, on a 4 mmol scale, to afford the product as a white solid (454 mg, 36.8%).

Mpt: 138-142 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.27 (m, 1H), 7.00 (m, 1H), 6.02 (dq, *J* = 2.0, 0.9 Hz, 1H), 5.02 (d, *J* = 2.0 Hz, 1H), 2.31 (app. t, *J* = 0.7 Hz, 3H), 2.27 (d, *J* = 0.9, 3H), 2.14 (app. t, *J* = 0.6 Hz, 3H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 169.0, 164.6, 163.6, 145.3, 137.9, 132.0, 131.8, 131.4, 115.7, 99.4, 90.1, 20.6, 20.1, 16.4; MS (ESI) *m/z* (rel.%): 333 [<sup>81</sup>Br-MNa<sup>+</sup>] (17), 331 [<sup>79</sup>Br-MNa<sup>+</sup>] (18), 311 [<sup>81</sup>Br-MH<sup>+</sup>] (97), 309 [<sup>79</sup>Br-MH<sup>+</sup>] (100); HRMS (ESI) calculated for C<sub>14</sub>H<sub>14</sub>BrO<sub>3</sub>: 309.0121, found: 309.0119; IR (neat): 3074, 2922, 1699, 1640, 1563, 1445, 1400, 1220, 1203, 1134, 981, 828 cm<sup>-1</sup>.

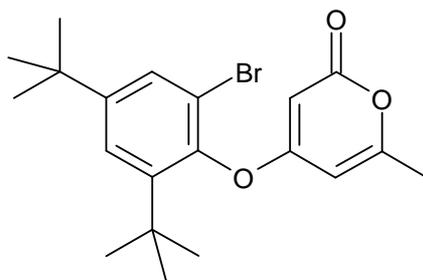
#### 4-(2-Bromo-4-*tert*-butylphenoxy)-6-methyl-2-pyrone (7e)



The title compound was prepared according to General Procedure A, on a 2 mmol scale, to afford the product as a white solid (442 mg, 65.6%).

Mpt: 148-149 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.60 (d, *J* = 2.2 Hz, 1H), 7.35 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 6.00 (d, *J* = 2.0 Hz, 1H), 5.06 (d, *J* = 2.0 Hz, 1H), 2.25 (s, 3H), 1.30 (s, 9H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 169.8, 164.4, 163.4, 151.7, 146.8, 131.0, 126.2, 122.4, 115.3, 99.6, 90.7, 34.7, 31.1, 20.0; MS (ESI) *m/z* (rel.%): 361 [<sup>81</sup>Br-MNa<sup>+</sup>] (20), 359 [<sup>79</sup>Br-MNa<sup>+</sup>] (22), 339 [<sup>81</sup>Br-MH<sup>+</sup>] (96), 337 [<sup>79</sup>Br-MH<sup>+</sup>] (100); HRMS (ESI) calculated for C<sub>16</sub>H<sub>18</sub>BrO<sub>3</sub>: 337.0434, found: 337.0425; IR (neat): 3089, 2955, 1707, 1644, 1567, 1491, 1440, 1403, 1225, 1132, 1047, 979, 858, 822 cm<sup>-1</sup>.

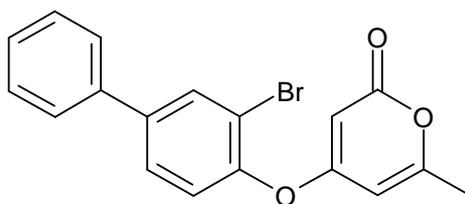
#### 4-(2-Bromo-4,6-di-*tert*-butyl-phenoxy)-6-methyl-2-pyrone (7f)



To a solution of 2-bromo-4,6-di-*tert*-butylphenol (285 mg, 1 mmol, 1 eq.) under nitrogen in THF (2 mL) was added NaH (24 mg, 1 mmol, 1eq.) in one portion. The solution was stirred at 25 °C for 1 hour then 4-bromo-6-methyl-2-pyrone (189 mg, 1 mmol, 1 eq.) was added and the solution stirred at 60 °C for 16 hours. The reaction was allowed to cool to ambient temperature and quenched by the addition of water (1 mL). The solution was then extracted by EtOAc (3 × 3 mL) and the combined organic extracts dried over MgSO<sub>4</sub>, concentrated in vacuo to afford the crude product. Purification by flash column chromatography (15% EtOAc in hexanes) afforded the title compound as a white solid (108.4mg, 27.6%).

Mpt: 108-110 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.45 (d, *J* = 2.3 Hz, 1H), 7.38 (d, *J* = 2.3 Hz, 1H), 5.99 (s, 1H), 5.05 (s, 1H), 2.27 (s, 3H), 1.31 (s, 9H), 1.30 (s, 9H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 169.7, 164.6, 163.5, 150.5, 145.2, 143.5, 129.1, 124.3, 117.2, 99.7, 91.7, 35.6, 34.8, 31.2, 30.6, 20.1; MS (ESI) *m/z* (rel.%): 417 [<sup>81</sup>Br-MNa<sup>+</sup>] (17), 415 [<sup>79</sup>Br-MNa<sup>+</sup>] (17), 395 [<sup>81</sup>Br-MH<sup>+</sup>] (100), 393 [<sup>79</sup>Br-MH<sup>+</sup>] (98); HRMS (ESI) calculated for C<sub>20</sub>H<sub>26</sub>BrO<sub>3</sub>: 393.1060, found: 393.1055; IR (neat): 2959, 1719, 1649, 1566, 1438, 1401, 1223, 1128, 979, 852, 826 cm<sup>-1</sup>.

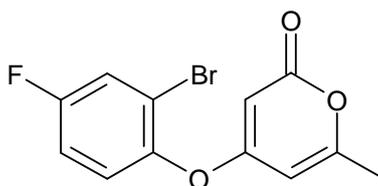
#### 4-(2-Bromo-4-phenyl-phenoxy)-6-methyl-2-pyrone (7g)



The title compound was prepared according to General Procedure A, on a 2 mmol scale, to afford the product as a white solid (646 mg, 90.4%).

Mpt: 125-127 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.86 (d, *J* = 2.2 Hz, 1H), 7.57 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.53 – 7.56 (m, 2H), 7.44 – 7.49 (m, 2H), 7.40 (m, 1H), 7.20 (d, *J* = 8.4 Hz, 1H), 6.05 (dq, *J* = 2.2, 0.8 Hz, 1H), 5.17 (dd, *J* = 2.2, 0.5 Hz, 1H), 2.29 (dd, *J* = 0.8, 0.5 Hz, 3H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 169.6, 164.4, 163.6, 148.5, 141.6, 138.5, 132.6, 129.0, 128.2, 127.8, 127.1, 123.2, 116.2, 99.5, 91.1, 20.1; MS (ESI) *m/z* (rel.%): 381 [<sup>81</sup>Br-MNa<sup>+</sup>] (14), 379 [<sup>79</sup>Br-MNa<sup>+</sup>] (14), 359 [<sup>81</sup>Br-MH<sup>+</sup>] (98), 357 [<sup>79</sup>Br-MH<sup>+</sup>] (100); HRMS (ESI) calculated for C<sub>18</sub>H<sub>14</sub>BrO<sub>3</sub>: 357.0121, found: 357.0117; IR (neat): 3060, 1717, 1692, 1644, 1566, 1474, 1402, 1227, 1132, 1044, 982, 858, 817, 769, 738, 698 cm<sup>-1</sup>.

#### 4-(2-Bromo-4-fluoro-phenoxy)-6-methyl-2-pyrone (7h)



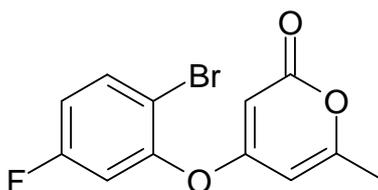
The title compound was prepared according to General Procedure A, on a 1 mmol scale, to afford the product as a white solid (260 mg, 87.1%).

Mpt: 112-113 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.41 (ddd, *J* = 7.5, 2.5, 0.7 Hz, 1H), 7.15 – 7.08 (m, 2H), 6.01 (dq, *J* = 0.8, 2.1 Hz, 1H), 5.06 (d, *J* = 2.1 Hz, 1H), 2.28 (d, *J* = 0.8 Hz, 3H);

<sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 169.53, 163.75, 162.8 (d, *J* = 273.1 Hz), 158.97, 145.7 (d, *J* = 3.6 Hz), 123.9 (d, *J* = 9.0 Hz), 121.3 (d, *J* = 26.0 Hz), 116.5 (d, *J* = 10.2 Hz), 116.1 (d, *J* = 23.3 Hz), 99.40, 90.98, 20.09;

<sup>19</sup>F-NMR (376 MHz, CDCl<sub>3</sub>): -112.45 (td, *J* = 7.5, 5.4 Hz); MS (ESI) *m/z* (rel.%): 301 [<sup>81</sup>Br-MH<sup>+</sup>] (97), 299 [<sup>79</sup>Br-MH<sup>+</sup>] (100); HRMS (ESI) calculated for C<sub>12</sub>H<sub>9</sub>BrFO<sub>3</sub>: 298.9714, found: 298.9714; IR (neat): 3065, 1731, 1651, 1568, 1480, 1443, 1402, 1246, 1182, 1134, 980, 851, 827, 783 cm<sup>-1</sup>.

#### 4-(2-Bromo-5-fluoro-phenoxy)-6-methyl-2-pyrone (7i)

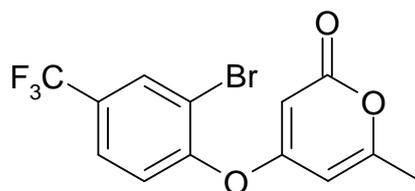


The title compound was prepared according to General Procedure A, on a 1 mmol scale, to afford the product as a white solid (262 mg, 87.7%).

Mpt: 120-122 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.62 (dd, *J* = 8.9, 5.7 Hz, 1H), 6.97 (ddd, *J* = 8.9, 7.7, 2.9, 1H), 6.92 (dd, *J* = 8.4, 2.9 Hz, 1H), 6.01 (dq, *J* = 2.1, 0.8 Hz, 1H), 5.10 (d, *J* = 2.1 Hz, 1H), 2.28 (d, *J* = 0.7 Hz, 3H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 169.0, 164.1, 163.9, 162.2 (d, *J* = 251.2 Hz), 150.0 (d, *J* = 10.6 Hz),

134.8 (d, *J* = 9.0 Hz), 115.5 (d, *J* = 22.2 Hz), 111.2 (d, *J* = 24.9 Hz), 110.59 (d, *J* = 4.2 Hz), 99.3, 91.3, 20.1; <sup>19</sup>F-NMR (376 MHz, CDCl<sub>3</sub>): -110.01 (td, *J* = 8.0, 5.7 Hz); MS (ESI) *m/z* (rel.%): 301 [<sup>81</sup>Br-MH<sup>+</sup>] (97), 299 [<sup>79</sup>Br-MH<sup>+</sup>] (100); HRMS (ESI) calculated for C<sub>12</sub>H<sub>9</sub>BrFO<sub>3</sub>: 298.9714, found: 298.9711; IR (neat): 3063, 2923, 2855, 1726, 1644, 1563, 1453, 1401, 1233, 1166, 1134, 995, 947, 851, 808 cm<sup>-1</sup>.

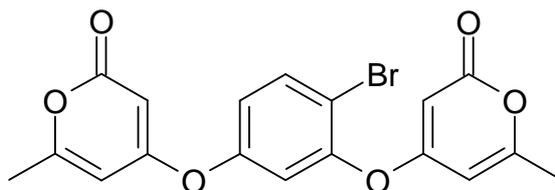
#### 4-(2-Bromo-4-(trifluoromethyl)-phenoxy)-6-methyl-2-pyrone (7j)



The title compound was prepared according to General Procedure A, on a 0.5 mmol scale, to afford the product as a white solid (166.4 mg, 95.3%).

Mpt: 91-93 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.93 (dq, *J* = 2.2, 0.7 Hz, 1H), 7.65 (ddq, *J* = 8.4, 2.2, 0.7 Hz, 1H), 7.26 (dq, *J* = 8.4, 0.8 Hz, 1H), 6.02 (dq, *J* = 2.3, 0.9 Hz, 1H), 5.07 (dq, *J* = 2.3, 0.6 Hz, 1H), 2.27 (dd, *J* = 0.9, 0.6 Hz, 3H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 168.8, 164.1, 163.9, 152.1, 131.6 (q, *J* = 3.7 Hz), 130.3 (q, *J* = 33.9 Hz), 127.7 (q, *J* = 3.6 Hz), 126.4 (q, *J* = 3.5 Hz), 123.6, 116.6, 99.3, 91.4, 20.1; <sup>19</sup>F-NMR (376 MHz, CDCl<sub>3</sub>): -62.38 (s); MS (ESI) *m/z* (rel.%): 351 [<sup>81</sup>Br-MH<sup>+</sup>] (96), 349 [<sup>79</sup>Br-MH<sup>+</sup>] (100), 282 (7), 271 (12); HRMS (ESI) calculated for C<sub>13</sub>H<sub>9</sub>BrF<sub>3</sub>O<sub>3</sub>: 348.9682, found: 348.9685; IR (neat): 3086, 2960, 2159, 1721, 1646, 1607, 1568, 1511, 1446, 1405, 1320, 1245, 1119, 1075, 982, 818 cm<sup>-1</sup>.

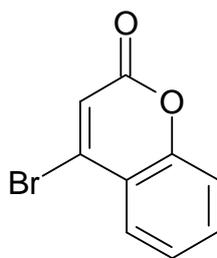
#### 1-Bromo-2,4-bis(6-methyl-2-pyronyl-4-oxy)-benzene (7k)



A solution of 4-bromo-6-methyl-2-pyrone (756 mg, 4 mmol, 2 eq.), 2-bromoresorcinol (378 mg, 2 mmol, 1 eq.), and K<sub>2</sub>CO<sub>3</sub> (690 mg, 5 mmol, 2.5 eq.) in acetone (4 ml/mmol) was stirred at 60 °C for 16 hours. The reaction was quenched by addition of water and ethyl acetate, and the layers separated. The aqueous layer was extracted 3 times using ethyl acetate and the combined organic extracts dried over MgSO<sub>4</sub>, concentrated *in vacuo* and purified by flash column chromatography (10-30 % EtOAc in hexanes) to afford the title compound as a white crystalline solid (395 mg, 48.8%).

Mpt: 143-146 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.72 (d, *J* = 8.7 Hz, 1H), 6.97 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.93 (d, *J* = 2.7 Hz, 1H), 6.02 (dq, *J* = 2.2, 0.9 Hz, 1H), 5.95 (dq, *J* = 2.2, 0.9 Hz, 1H), 5.27 (d, *J* = 2.2 Hz, 1H), 5.11 (d, *J* = 2.2 Hz, 1H), 2.28 (d, *J* = 0.9 Hz, 3H), 2.27 (d, *J* = 0.9 Hz, 3H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 169.5, 168.9, 164.0, 164.0, 163.9, 152.4, 150.4, 135.3, 120.8, 116.4, 113.3, 99.4, 99.3, 91.7, 91.3, 30.9, 20.1, 20.1; MS (ESI) *m/z* (rel.%): 429 [<sup>81</sup>Br-MNa<sup>+</sup>] (97), 427 [<sup>79</sup>Br-MNa<sup>+</sup>] (100), 407 [<sup>81</sup>Br-MH<sup>+</sup>] (90), 405 [<sup>79</sup>Br-MH<sup>+</sup>] (90); HRMS (ESI) calculated for C<sub>18</sub>H<sub>13</sub>BrNaO<sub>6</sub>: 426.9788, found: 426.9794; IR (neat): 3058, 1722, 1644, 1584, 1565, 1473, 1444, 1399, 1315, 1264, 1227, 1179, 1140, 982, 856, 812 cm<sup>-1</sup>.

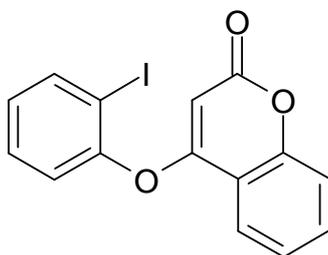
## 4-Bromo-coumarin<sup>6</sup>



A 250 ml 3-neck flask containing 4-hydroxy coumarin (1.49 g, 9.2 mmol, 1 eq.), P<sub>2</sub>O<sub>5</sub> (3.13 g, 22.1 mmol, 2.4 eq.) and TBAB (3.26 g, 10.1 mmol, 1.1 eq.) in toluene (100 ml) was equipped with a condenser and a mechanical stirrer. The reaction mixture was then heated to reflux for 8 hours whilst stirring then allowed to cool to ambient temperature. The toluene was decanted off, and the viscous black residue was extracted with toluene (3 × 40 ml). The combined organic fractions were concentrated *in vacuo* and recrystallisation (toluene) afforded the title compound as pale orange crystals (1.16 g, 56%).

Mpt: 92-93 °C (lit. 87-89 °C); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 7.83 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.59 (ddd, *J* = 8.3, 7.4, 1.6 Hz, 1H), 7.38 – 7.30 (m, 2H), 6.85 (s, 1H); <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>): 158.6, 152.4, 141.4, 133.1, 128.0, 124.9, 119.5, 118.9, 116.9; MS (ESI) *m/z* (rel.%): 227 [<sup>81</sup>Br-MH<sup>+</sup>] (100), 225 [<sup>79</sup>Br-MH<sup>+</sup>] (98); HRMS (ESI) calculated for C<sub>9</sub>H<sub>6</sub>BrO<sub>2</sub>: 224.9546, found: 224.9550.

## 4-(2-Iodophenoxy)-coumarin (7l)

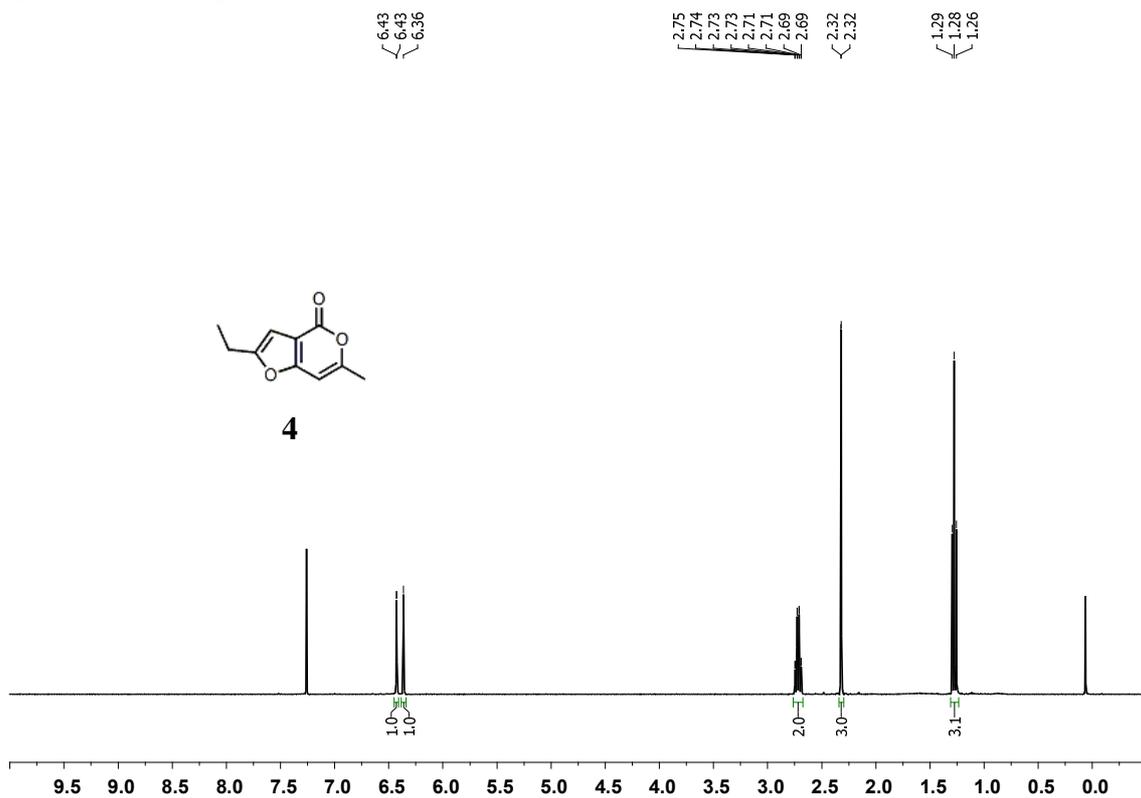


A solution of 4-bromo-coumarin (225 mg, 1 mmol, 1 eq.), 2-iodophenol (220 mg, 1 mmol, 1 eq.), and K<sub>2</sub>CO<sub>3</sub> (276 mg, 2 mmol, 2 eq.) in acetone (3 ml) was stirred at 60 °C for 16 hours. The reaction was allowed to cool to ambient temperature and quenched by addition of water (2 ml) and ethyl acetate (4 ml), and the layers separated. The aqueous layer was extracted using ethyl acetate (3 × 4 ml) and the combined organic extracts dried over MgSO<sub>4</sub>, concentrated *in vacuo* and purified by flash column chromatography (10-20 % EtOAc in hexanes) to afford the product as a white solid (310 mg, 85.1%).

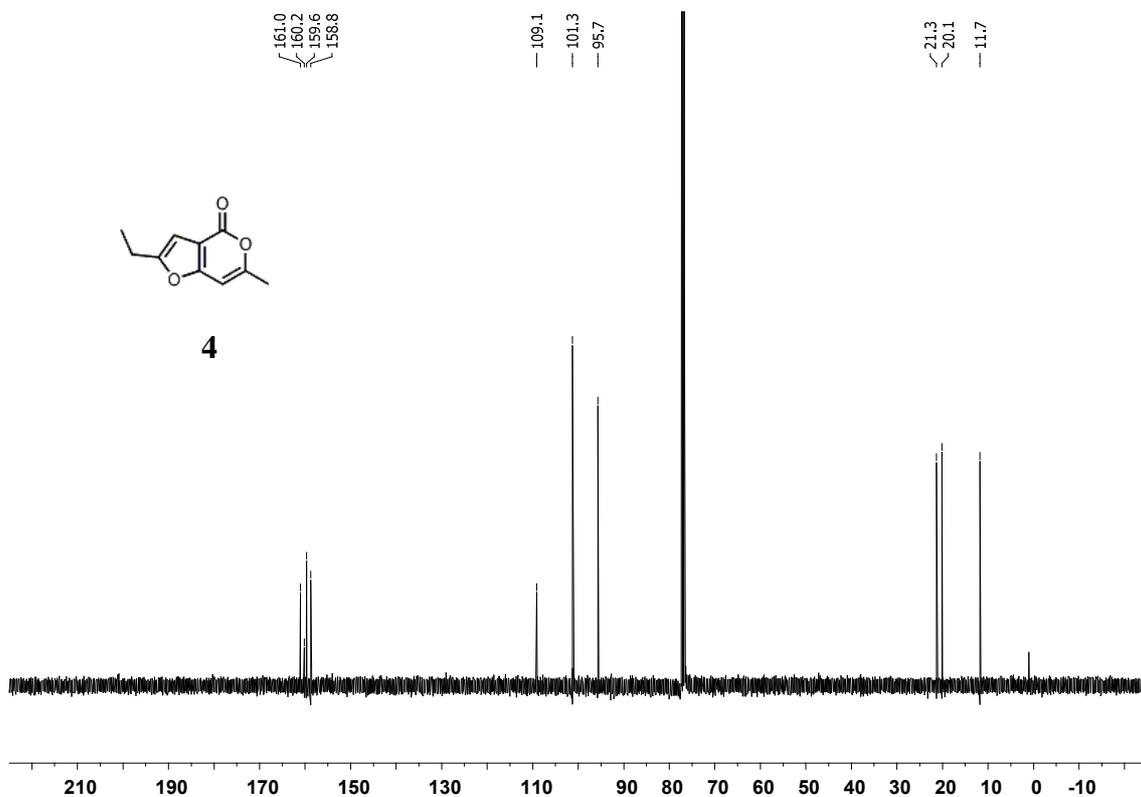
Mpt: 154-155 °C; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 8.09 (d, *J* = 7.5 Hz, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 7.5 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 5.31 (s, 1H); <sup>13</sup>C-NMR (126 MHz, CDCl<sub>3</sub>): 164.9, 162.4, 153.7, 152.3, 140.5, 132.9, 130.3, 128.5, 124.3, 123.3, 122.4, 116.9, 115.1, 93.8, 89.7; MS (ESI) *m/z* (rel.%): 387 [MNa<sup>+</sup>] (16), 365 [MH<sup>+</sup>] (100); HRMS (ESI) calculated for C<sub>15</sub>H<sub>10</sub>IO<sub>3</sub>: 364.9669, found: 364.9678; IR (neat): 3067, 1714, 1623, 1608, 1568, 1380, 1227, 1177, 1088, 929, 752 cm<sup>-1</sup>.

### 3. Representative NMR Spectra for Compounds

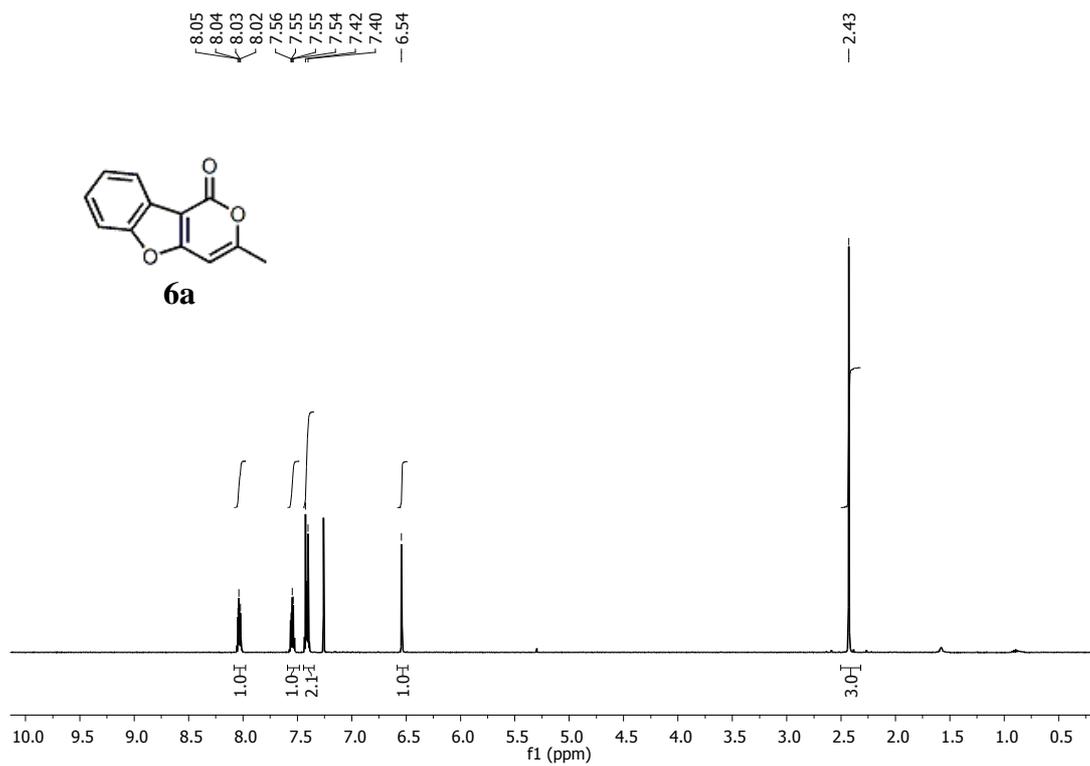
$^1\text{H}$  NMR spectrum of compound **4**.



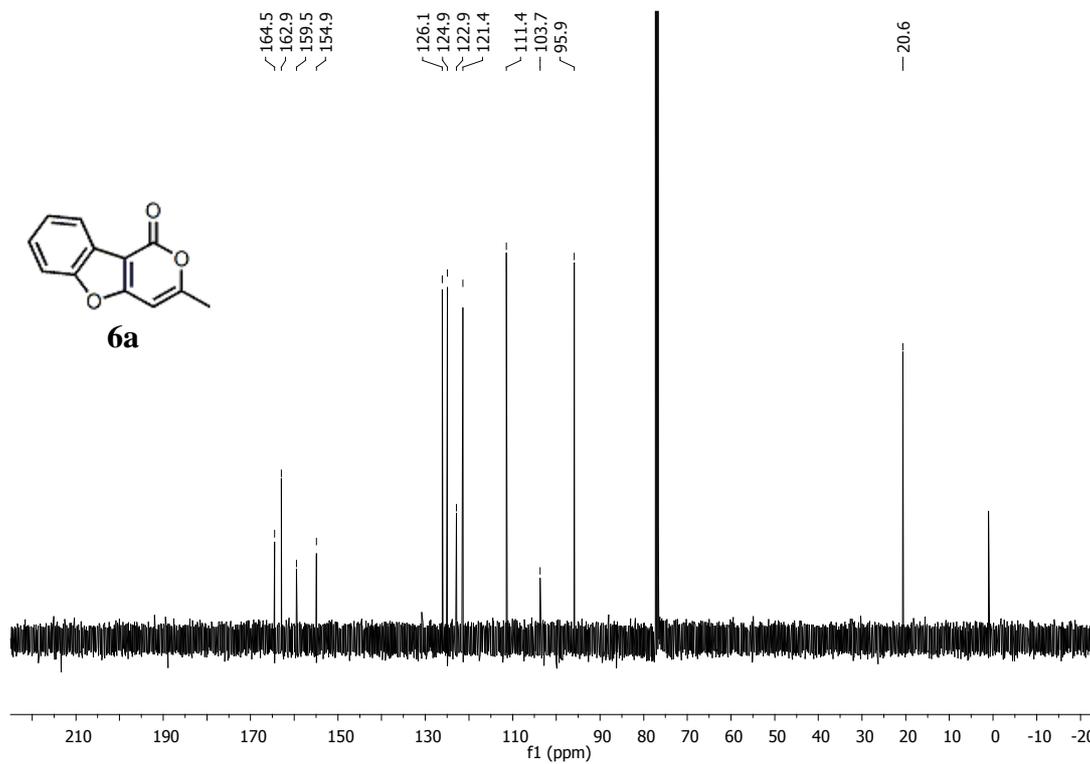
$^{13}\text{C}$  NMR spectrum of compound **4**.



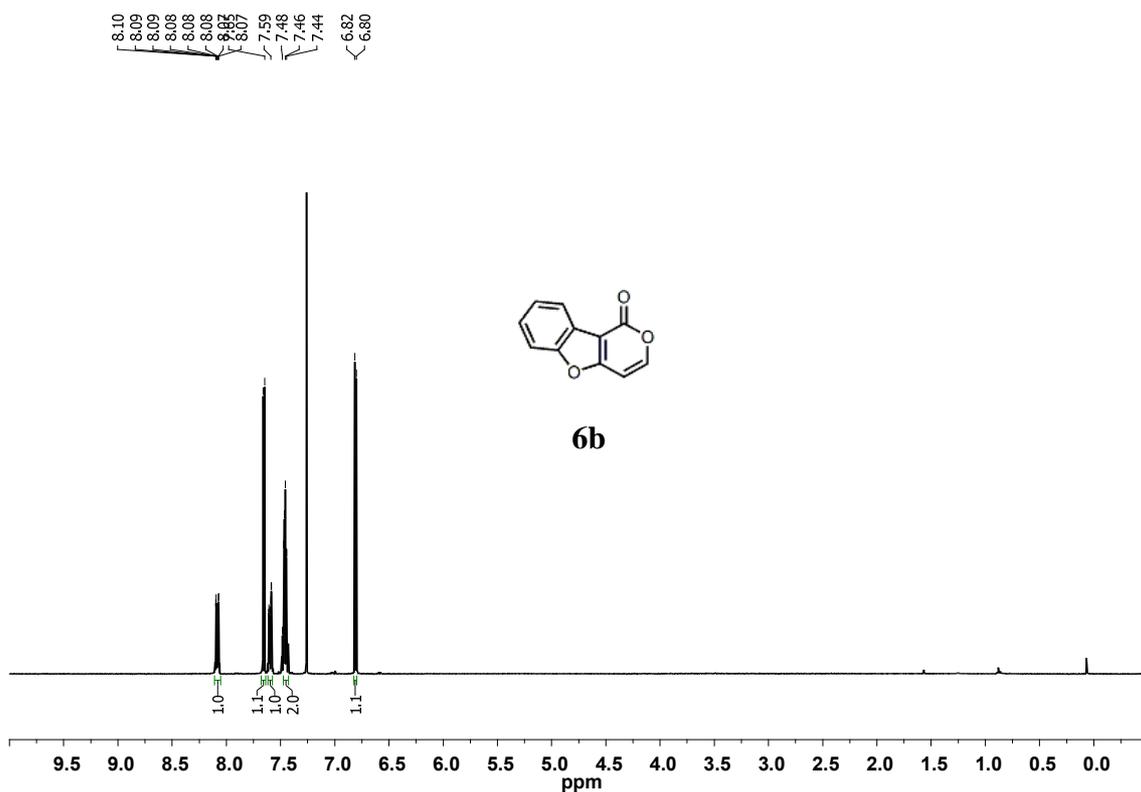
$^1\text{H}$  NMR spectrum of compound **6a**.



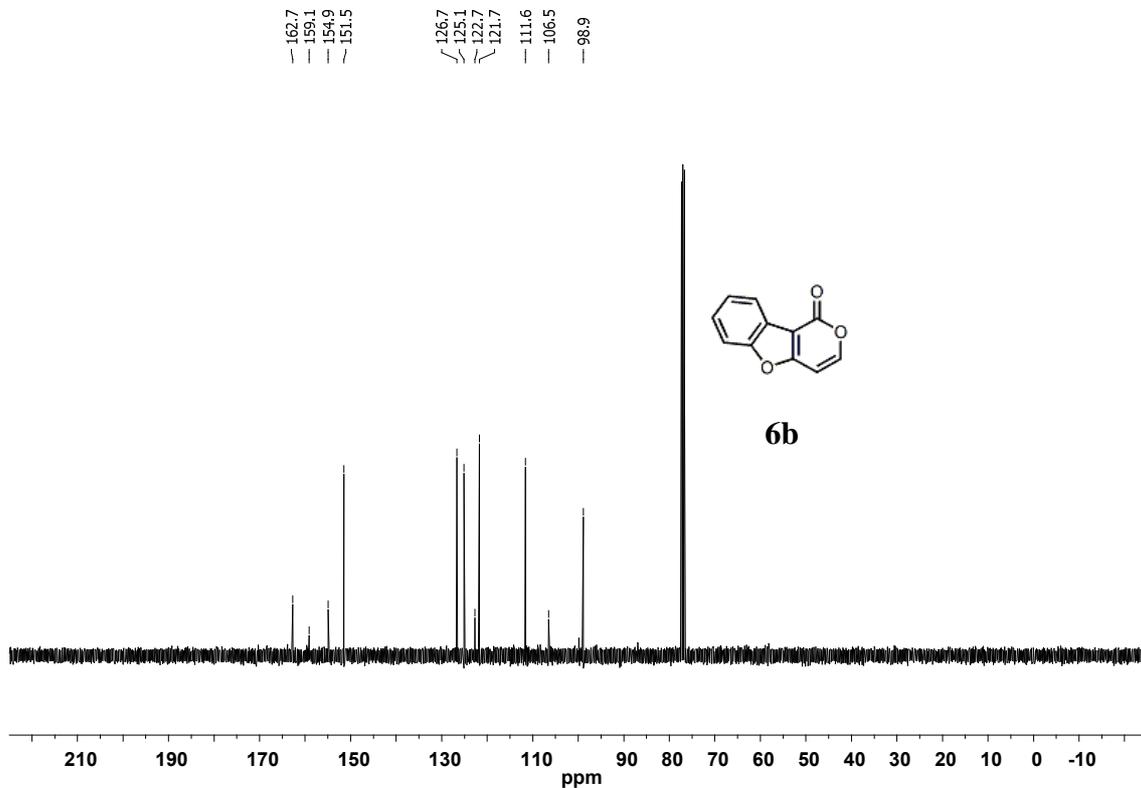
$^{13}\text{C}$  NMR spectrum of compound **6a**.



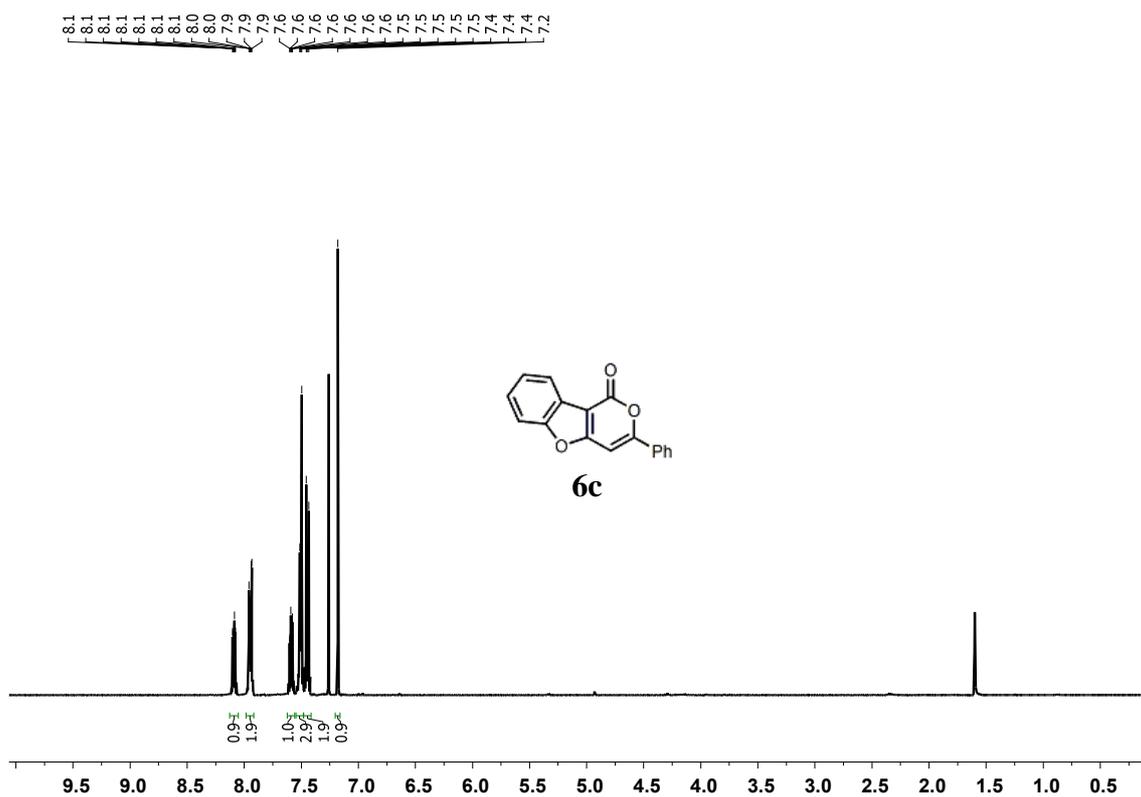
$^1\text{H}$  NMR spectrum of compound **6b**.



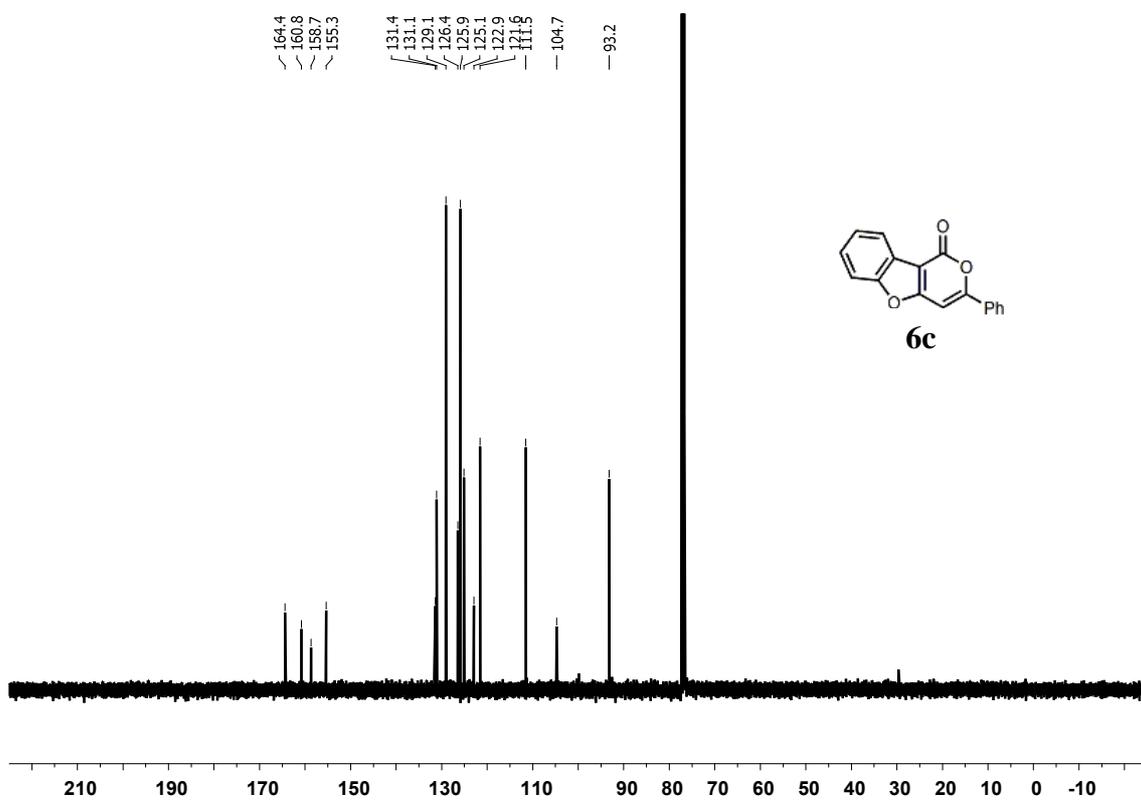
$^{13}\text{C}$  NMR spectrum of compound **6b**.



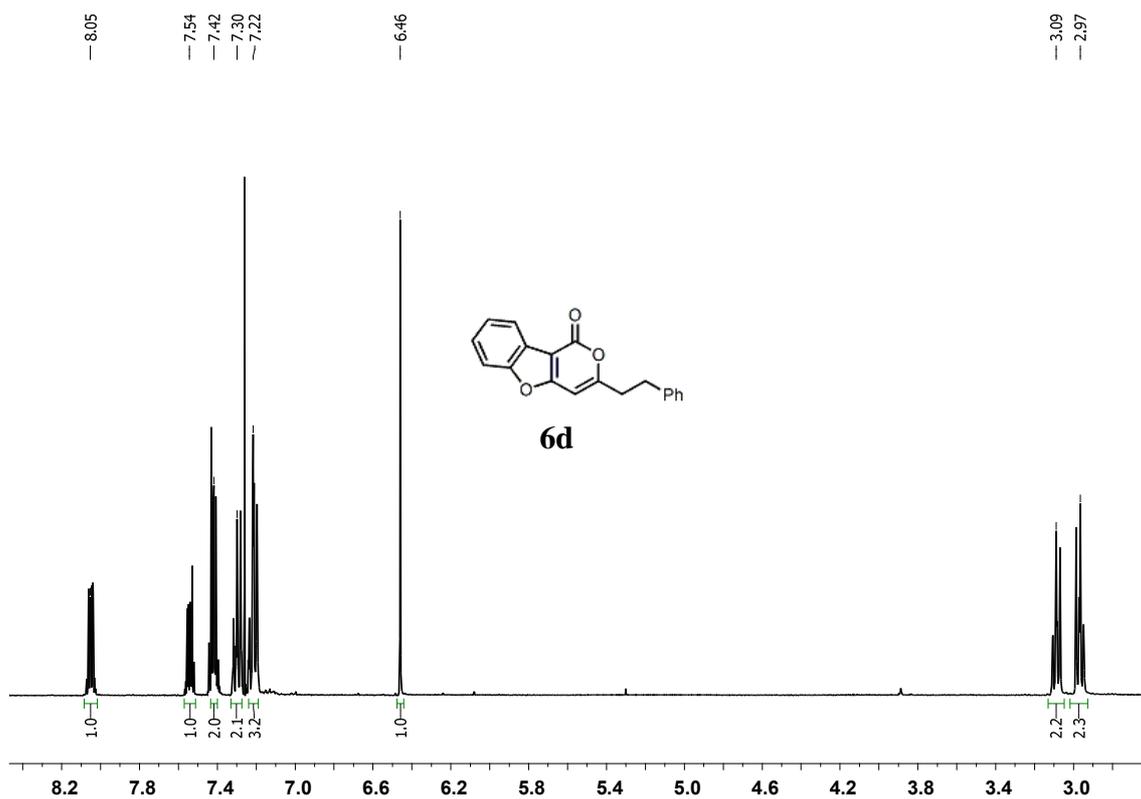
$^1\text{H}$  NMR spectrum of compound **6c**.



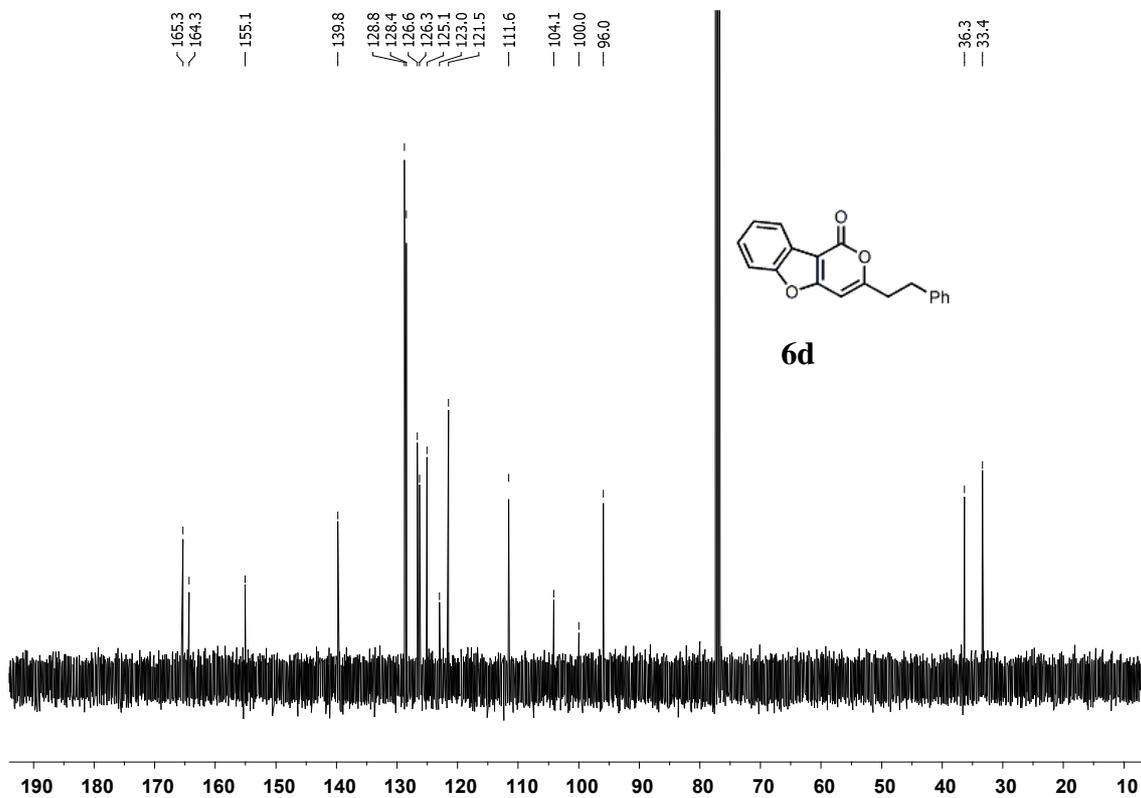
$^{13}\text{C}$  NMR spectrum of compound **6c**.



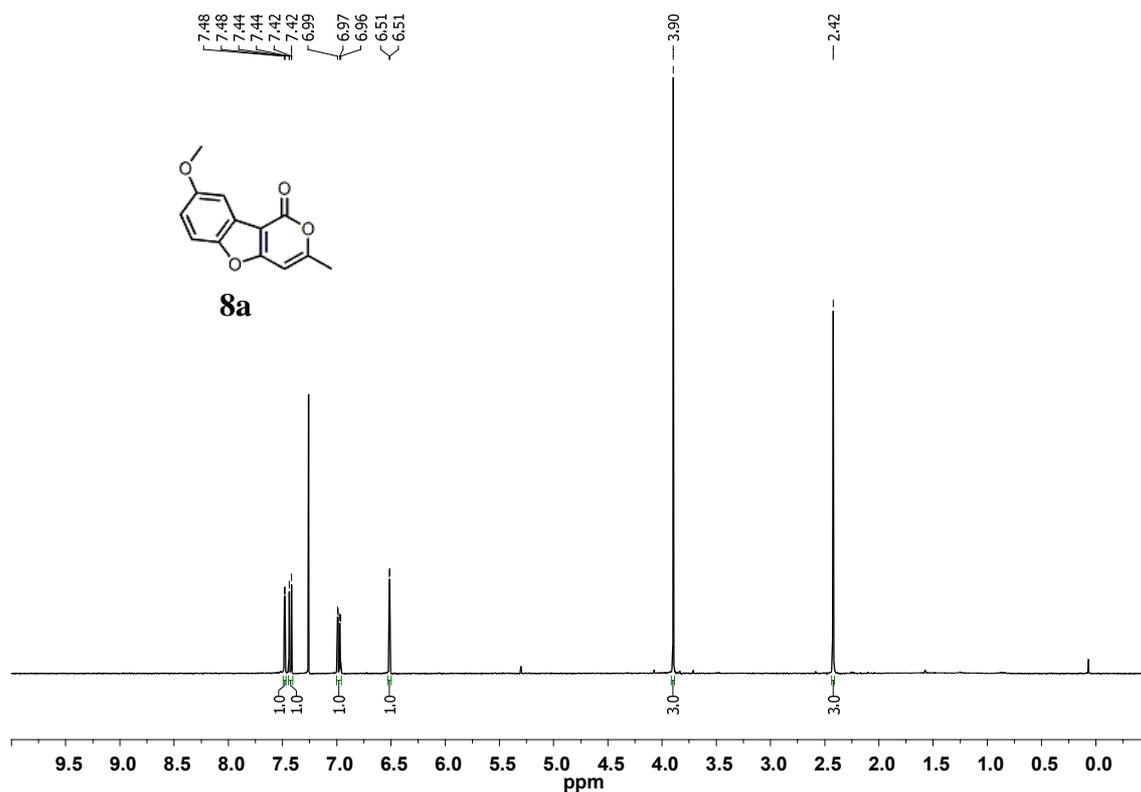
$^1\text{H}$  NMR spectrum of compound **6d**.



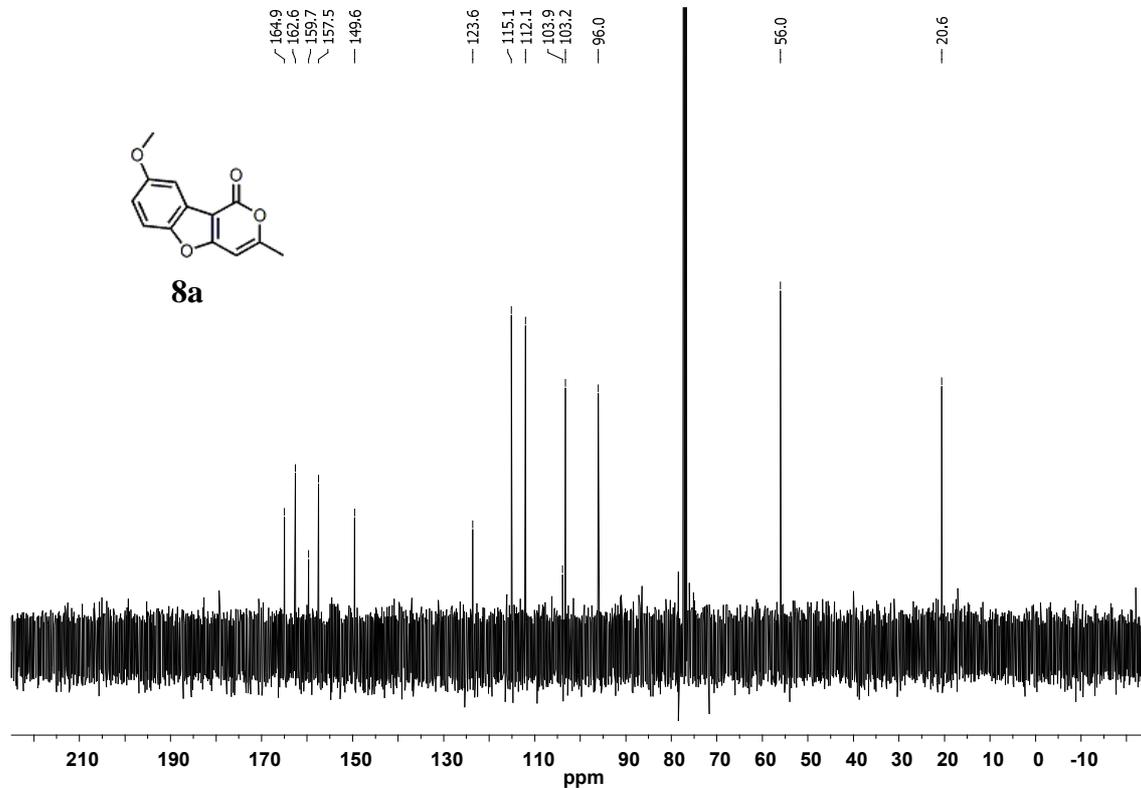
$^{13}\text{C}$  NMR spectrum of compound **6d**.



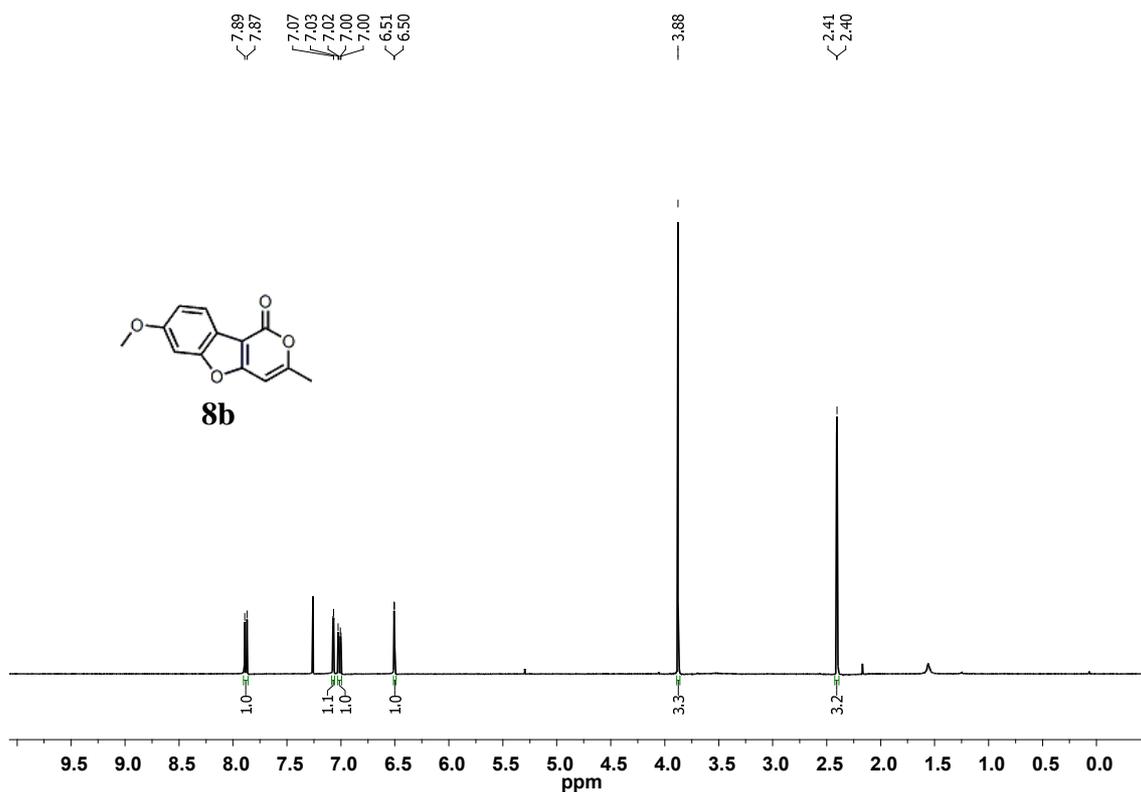
$^1\text{H}$  NMR spectrum of compound **8a**.



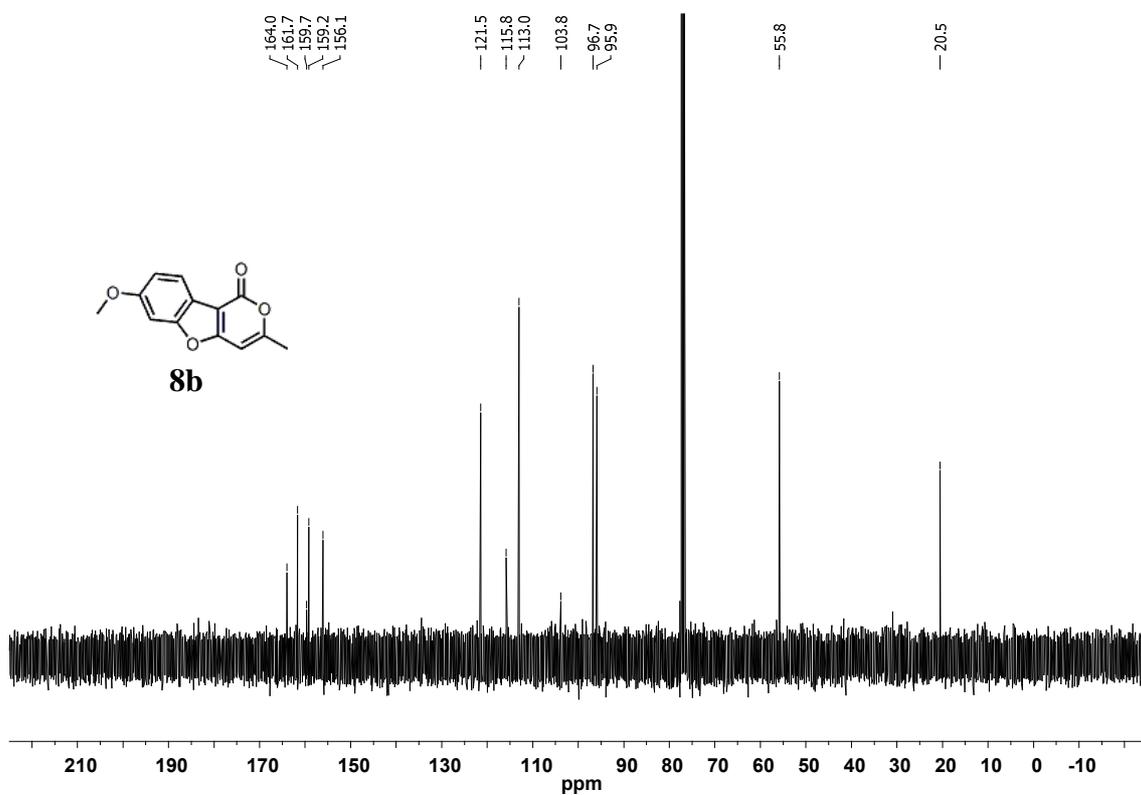
$^{13}\text{C}$  NMR spectrum of compound **8a**.



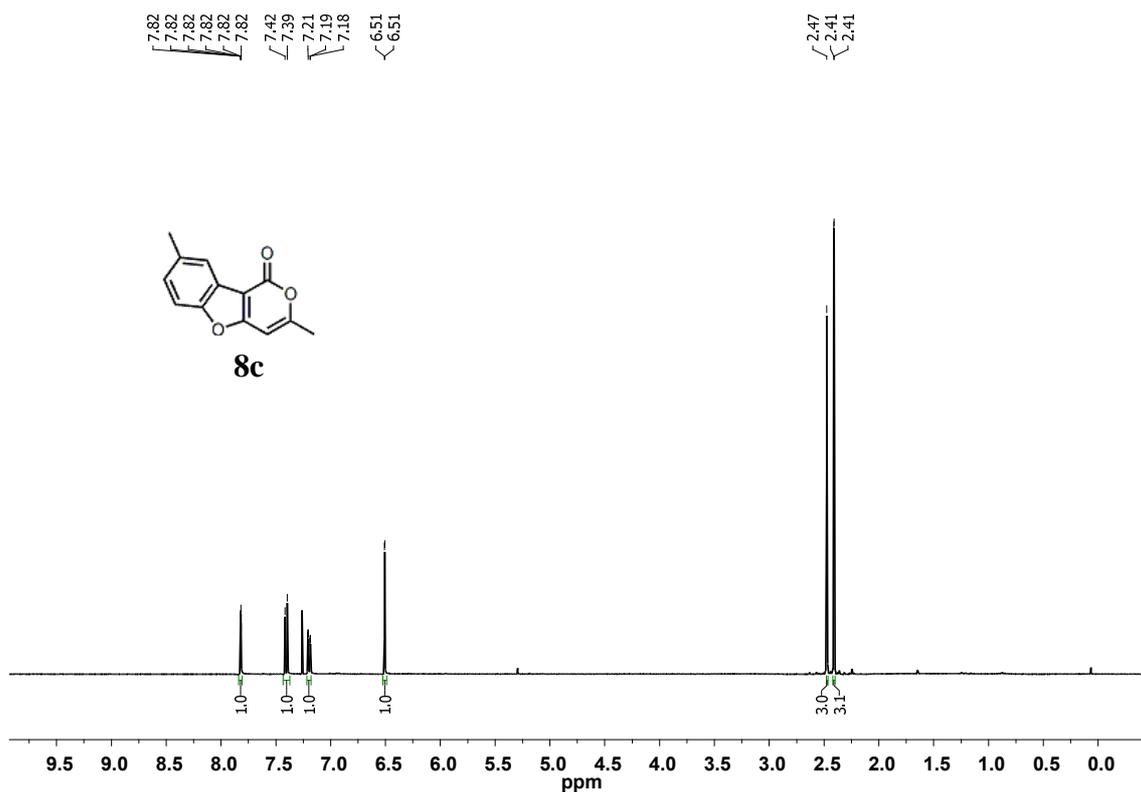
$^1\text{H}$  NMR spectrum of compound **8b**.



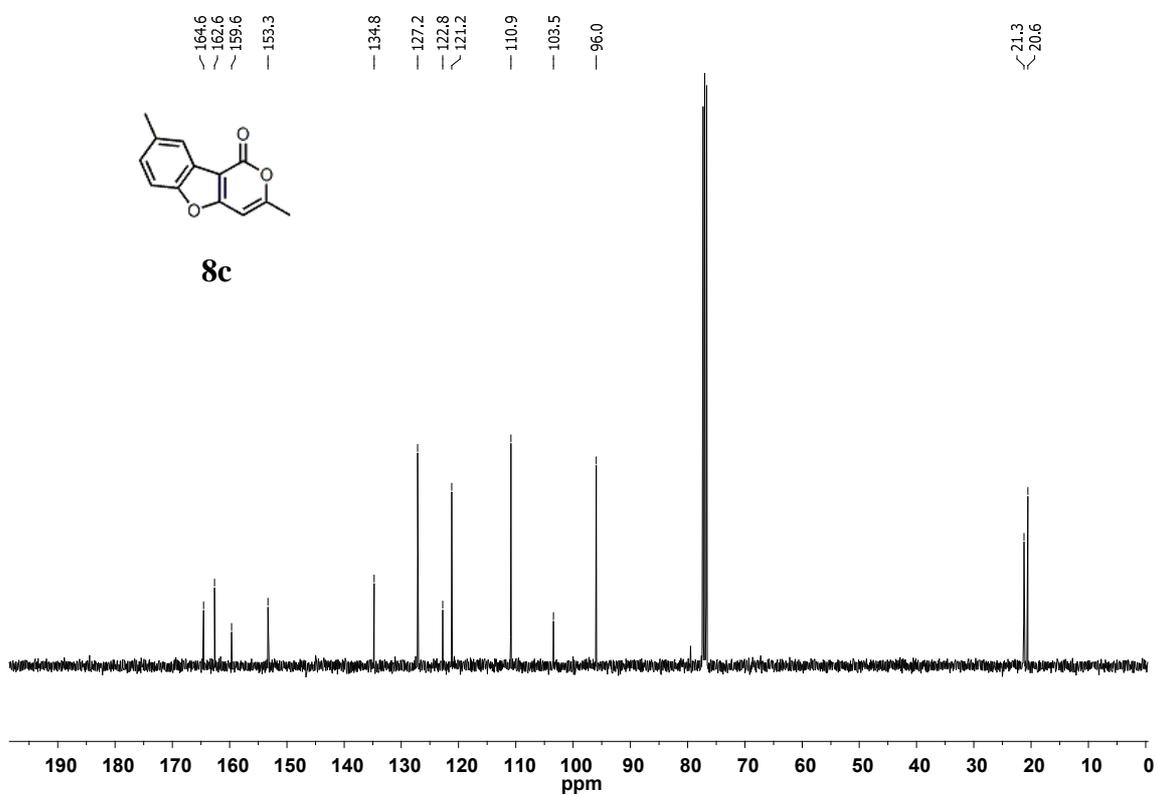
$^{13}\text{C}$  NMR spectrum of compound **8b**.



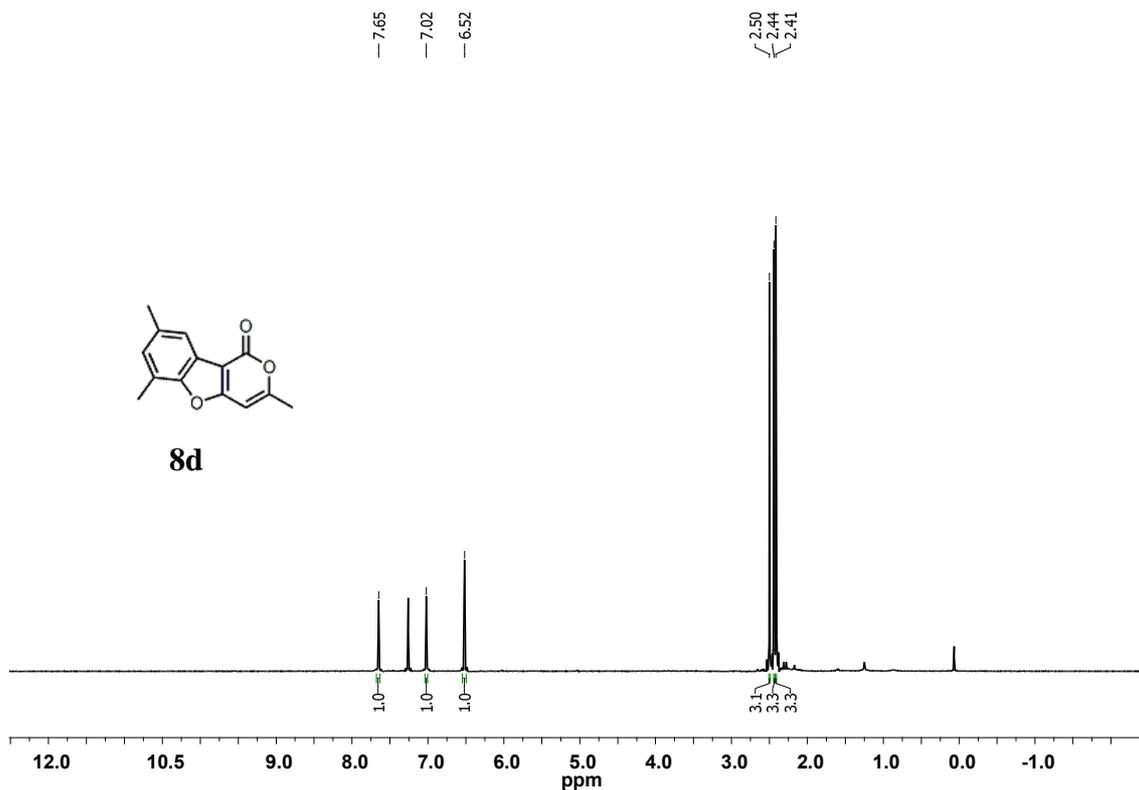
$^1\text{H}$  NMR spectrum of compound **8c**.



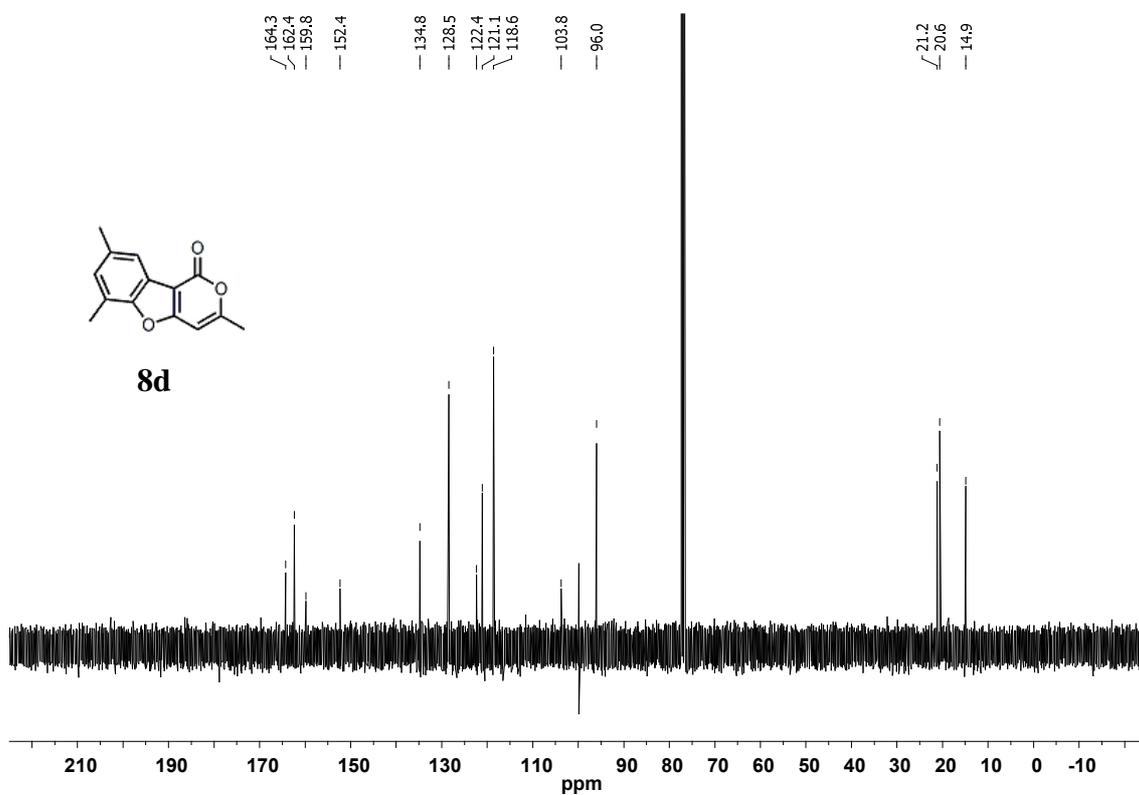
$^{13}\text{C}$  NMR spectrum of compound **8c**.



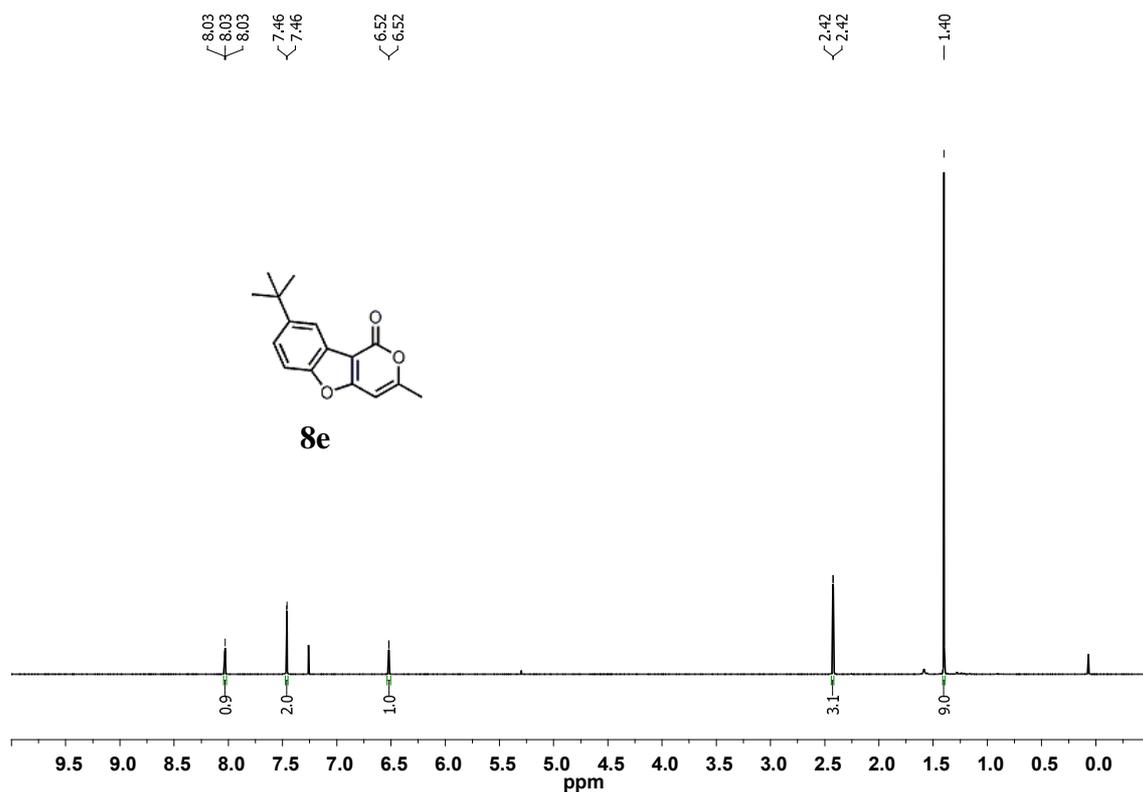
$^1\text{H}$  NMR spectrum of compound **8d**.



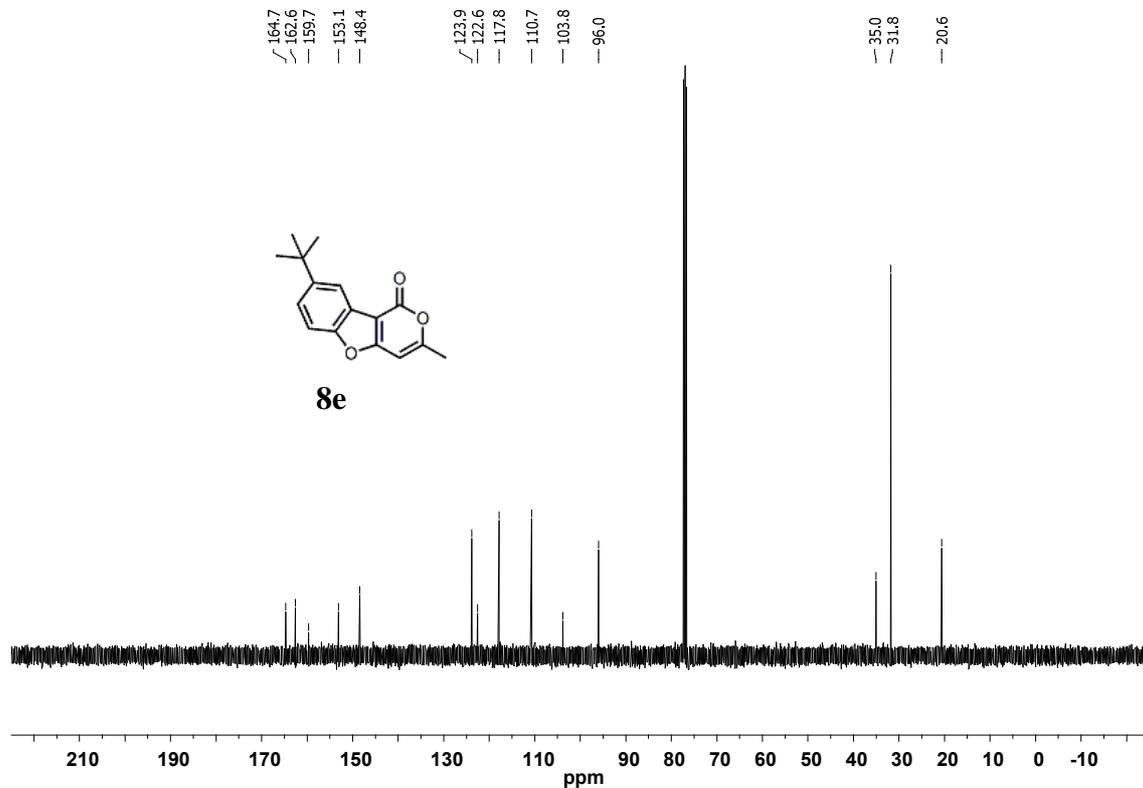
$^{13}\text{C}$  NMR spectrum of compound **8d**.



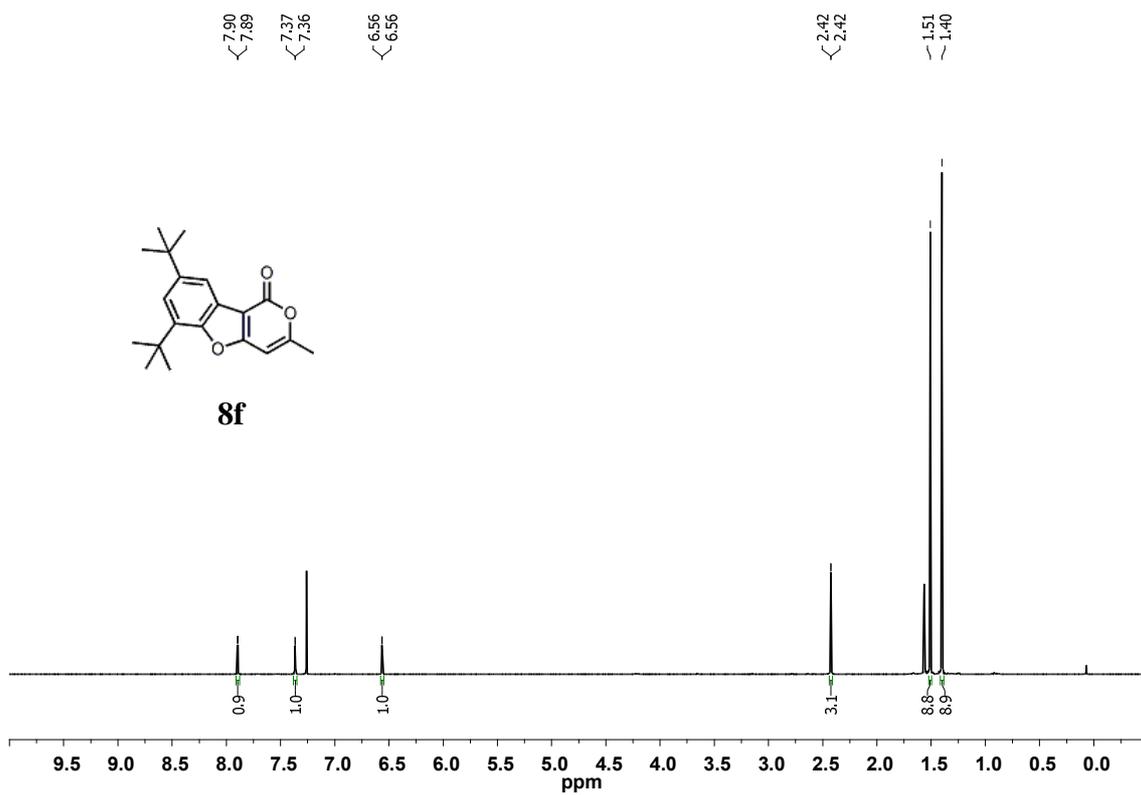
$^1\text{H}$  NMR spectrum of compound **8e**.



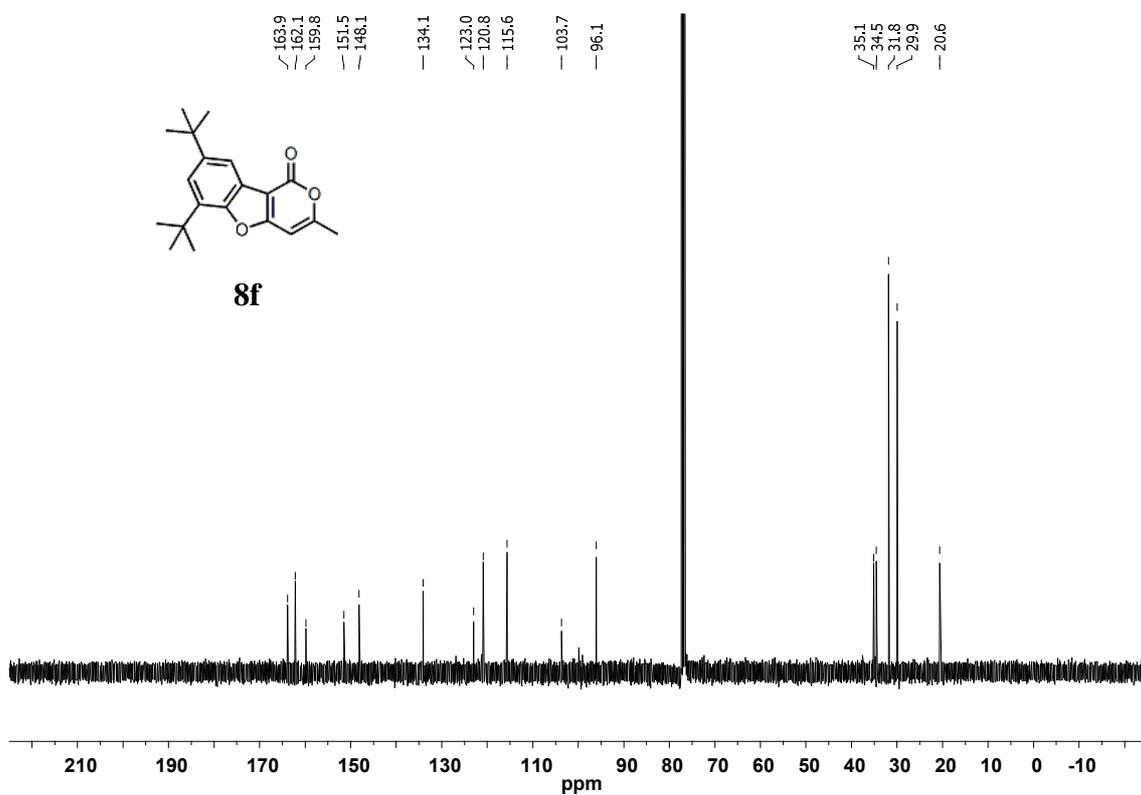
$^{13}\text{C}$  NMR spectrum of compound **8e**.



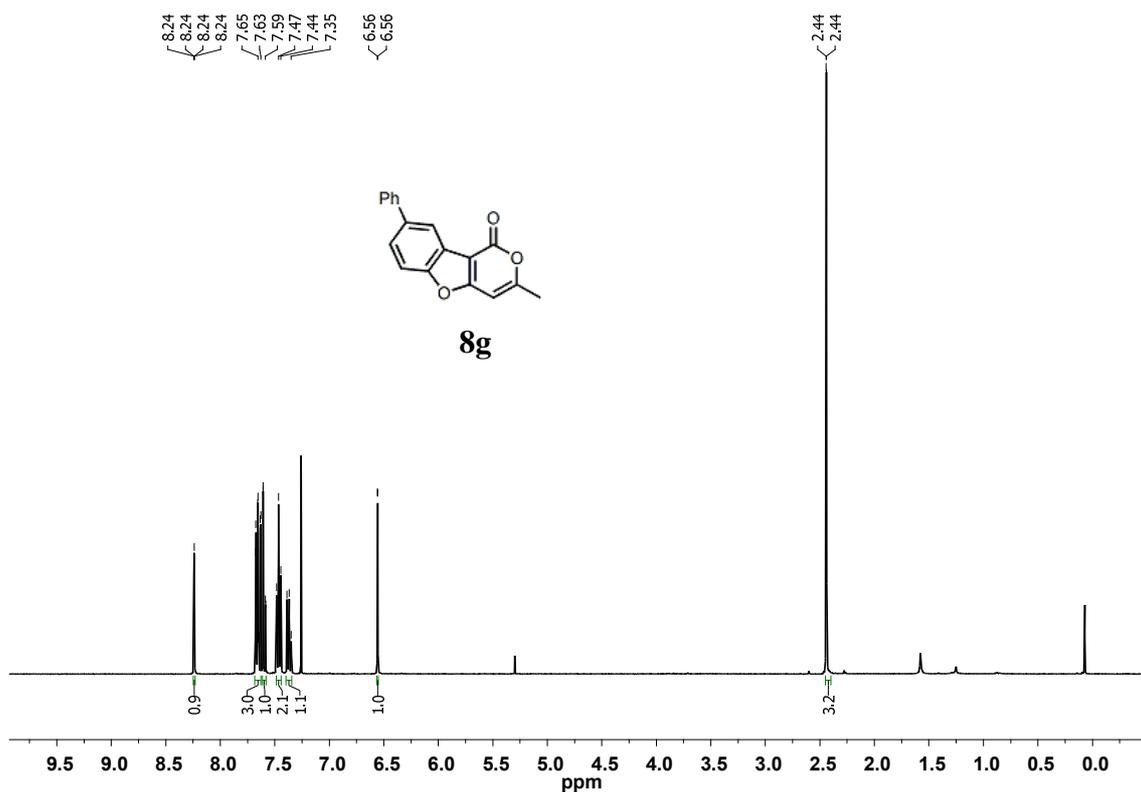
$^1\text{H}$  NMR spectrum of compound **8f**.



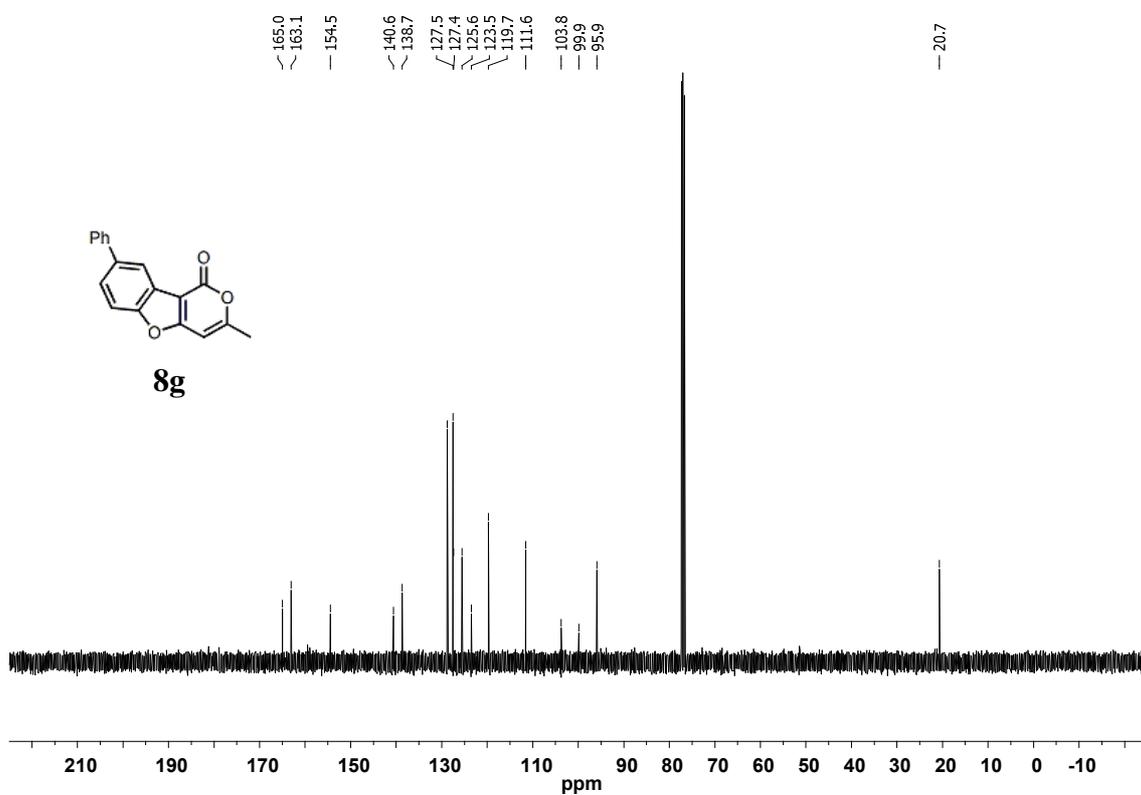
$^{13}\text{C}$  NMR spectrum of compound **8f**.



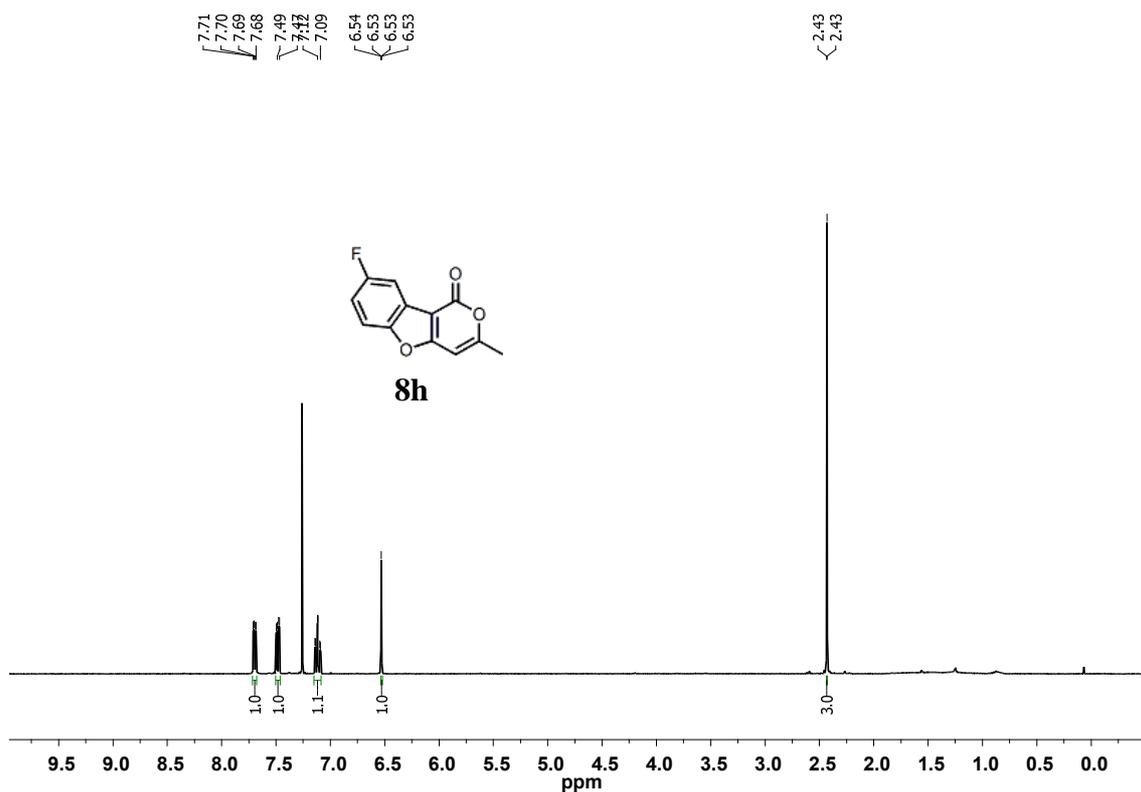
$^1\text{H}$  NMR spectrum of compound **8g**.



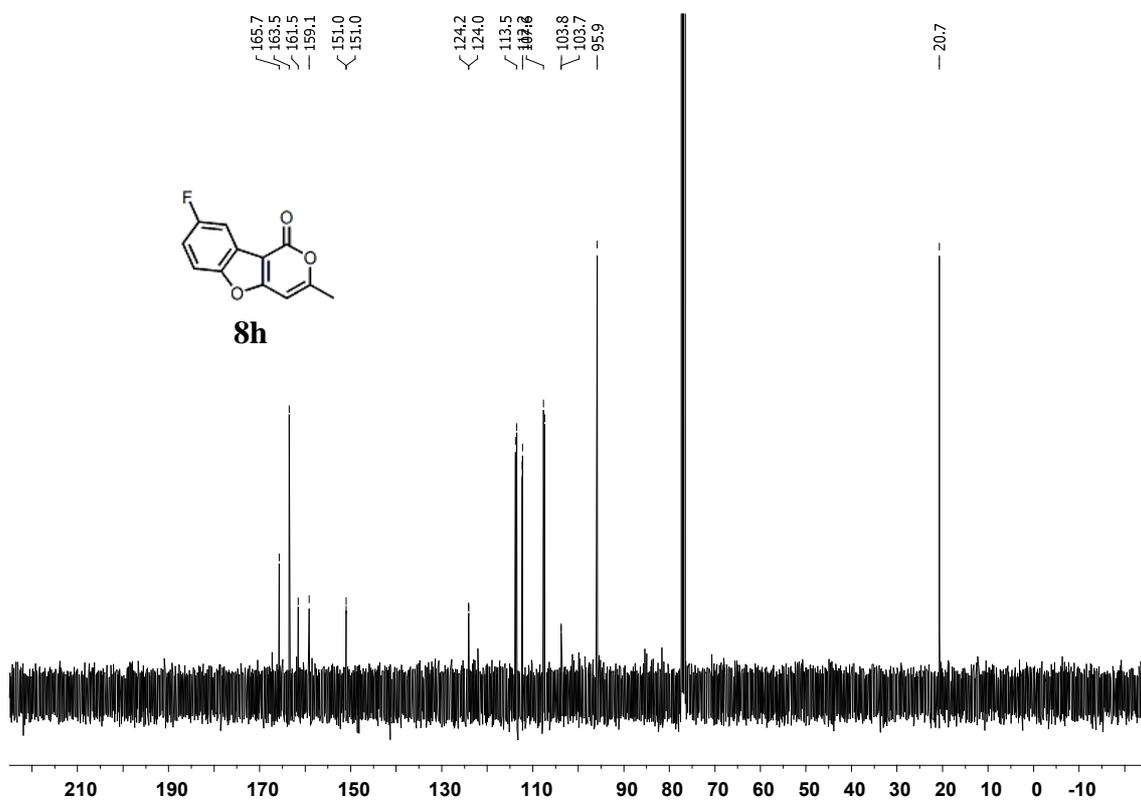
$^{13}\text{C}$  NMR spectrum of compound **8g**.



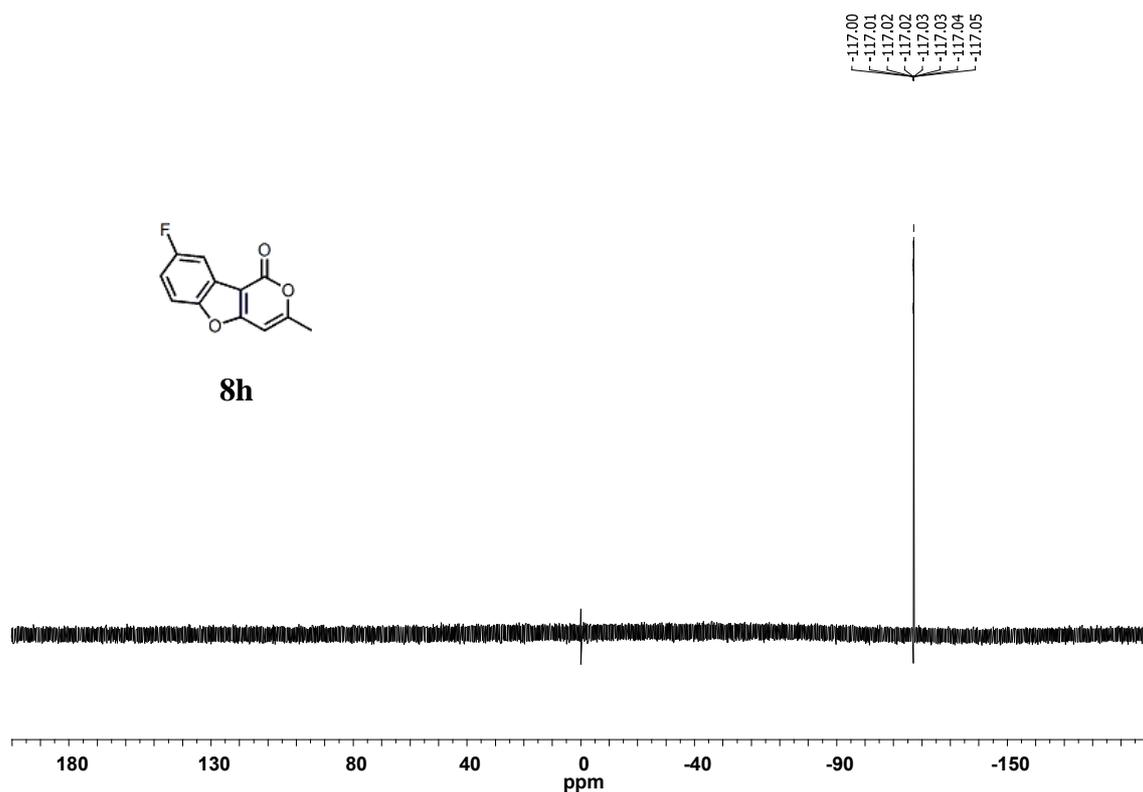
$^1\text{H}$  NMR spectrum of compound **8h**.



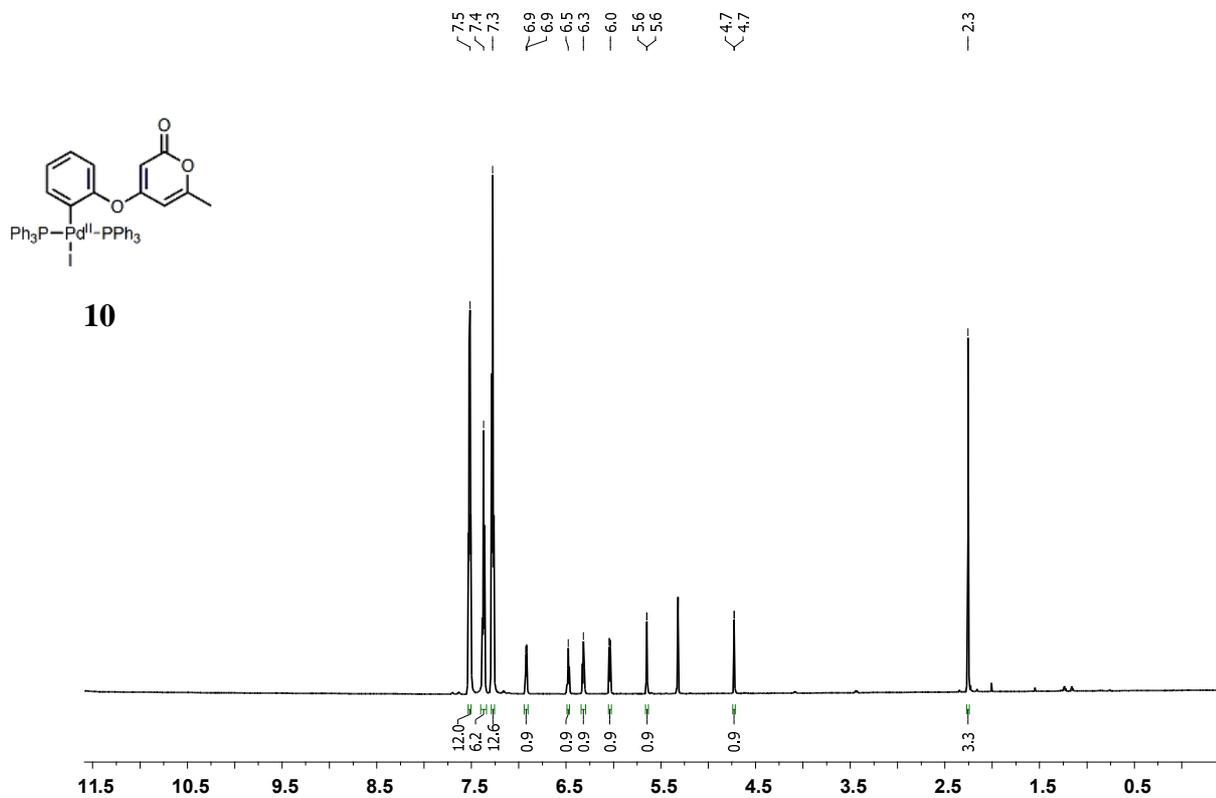
$^{13}\text{C}$  NMR spectrum of compound **8h**.



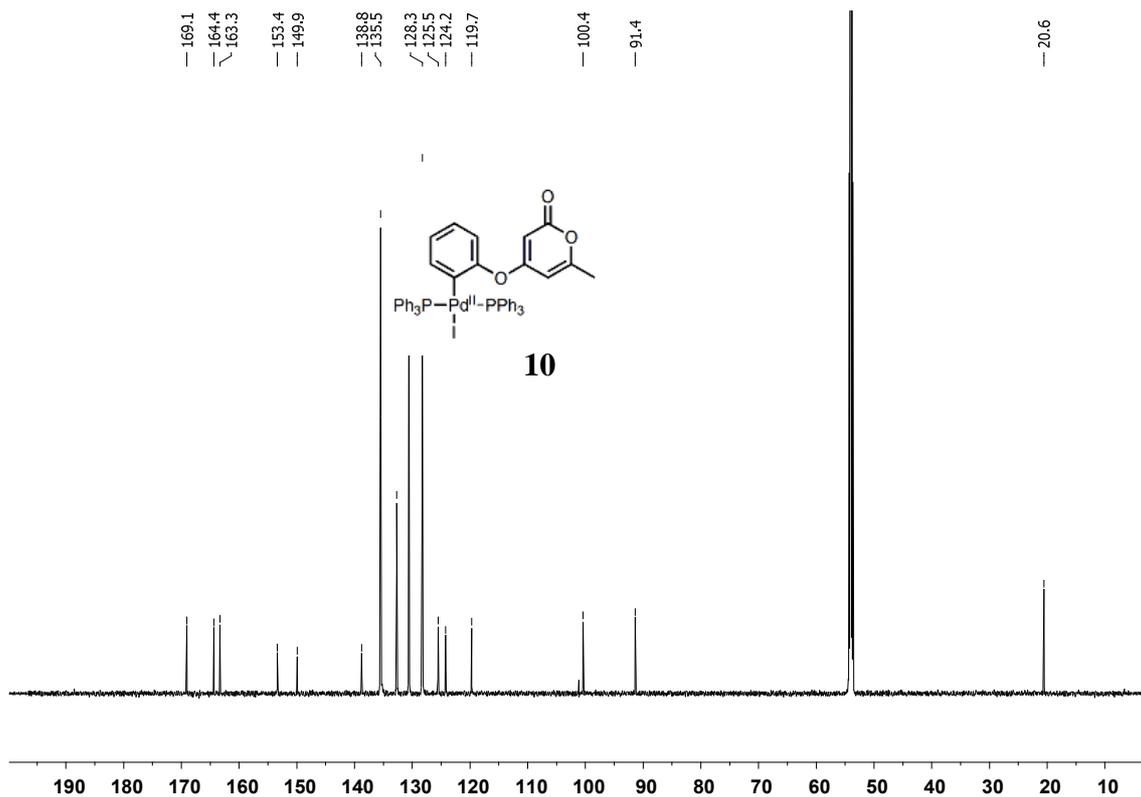
$^{19}\text{F}$  NMR spectrum of compound **8h**.



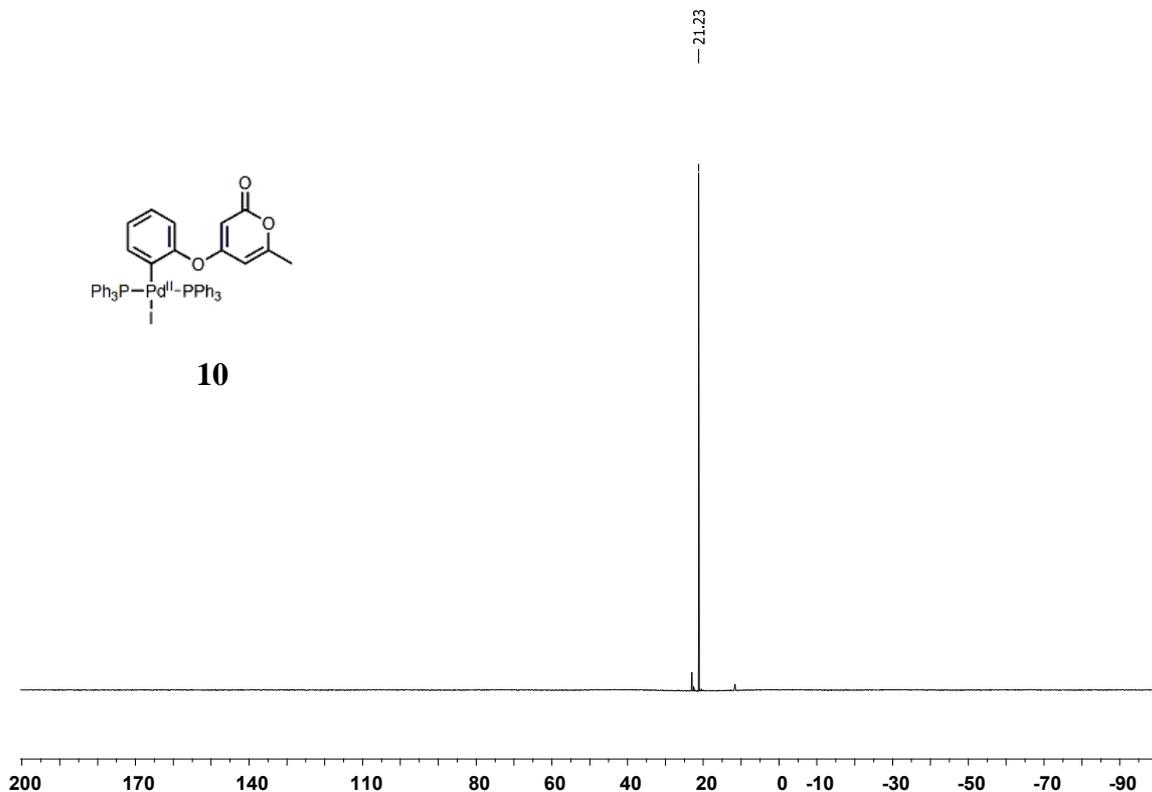
$^1\text{H}$  NMR spectrum of complex **10**.



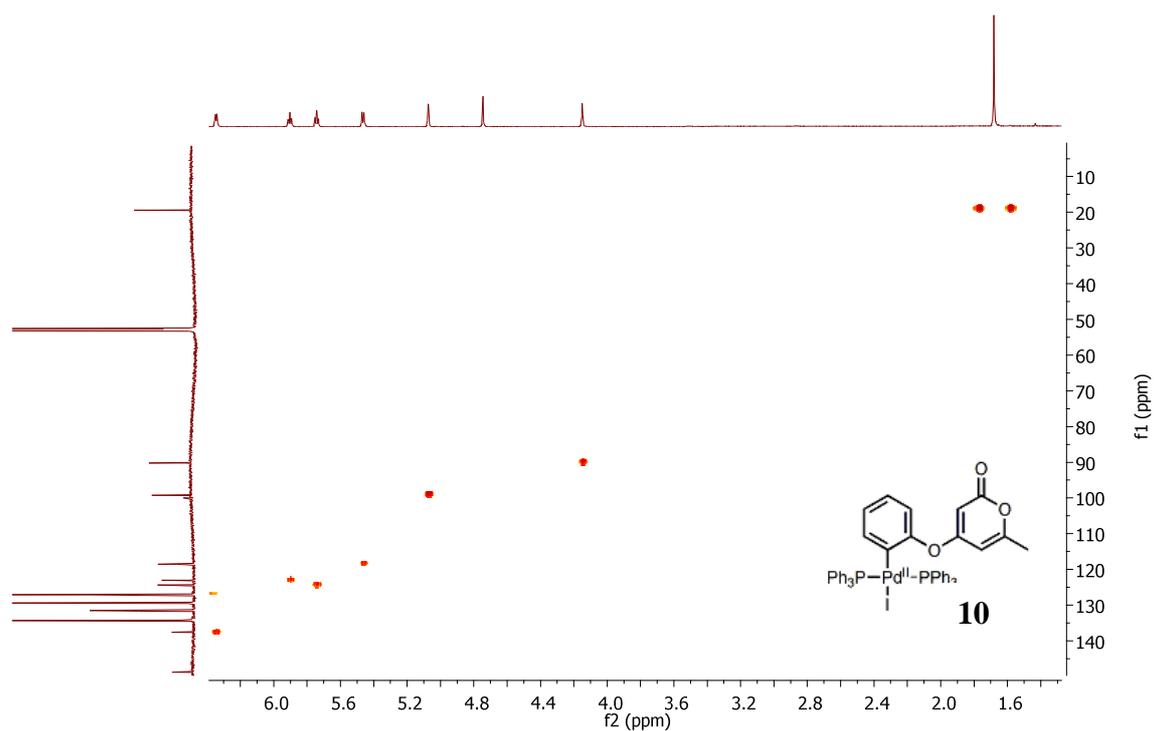
$^{13}\text{C}$  NMR spectrum of complex **10**.



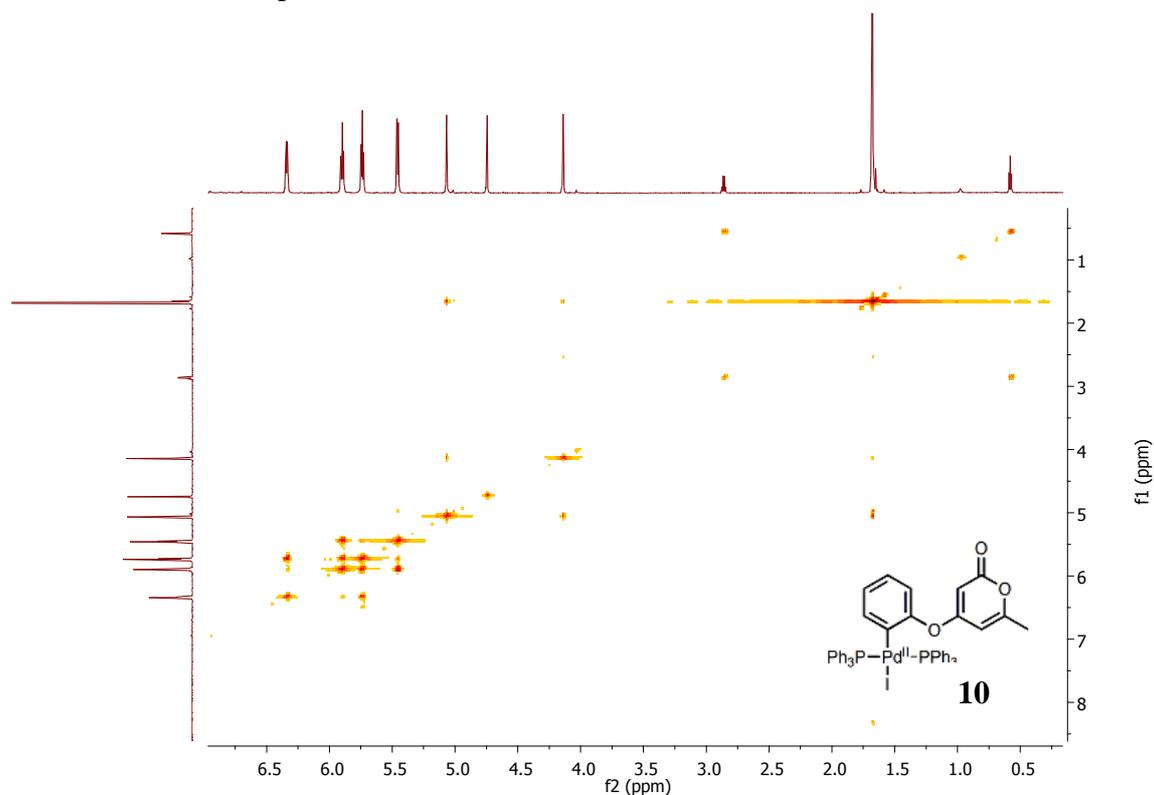
$^{31}\text{P}$  NMR spectrum of complex **10**.



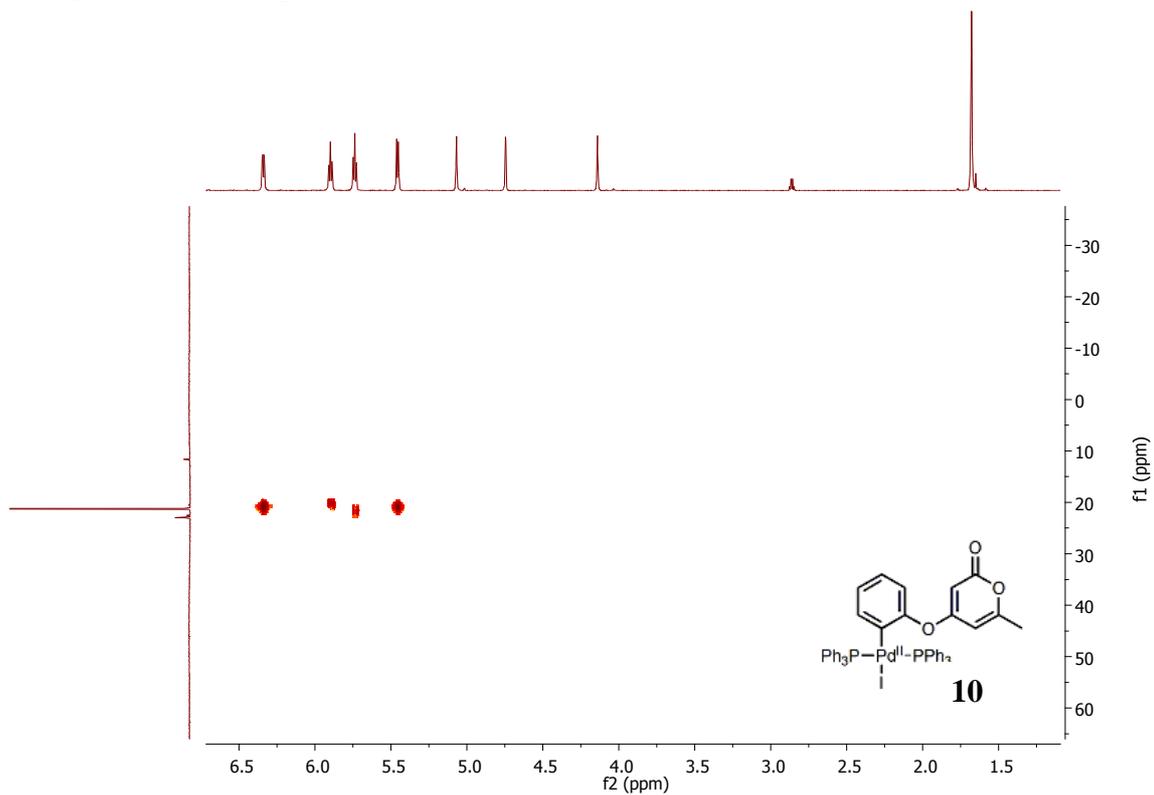
$^1\text{H}$ - $^{13}\text{C}$  2D HSQC NMR of complex **10** (700 MHz).



$^1\text{H}$ - $^1\text{H}$  2D COSY NMR of complex **10** (700 MHz).



$^1\text{H}$ - $^{31}\text{P}$  2D HSQC NMR of complex **10** (700 MHz).



#### 4. X-ray diffraction data

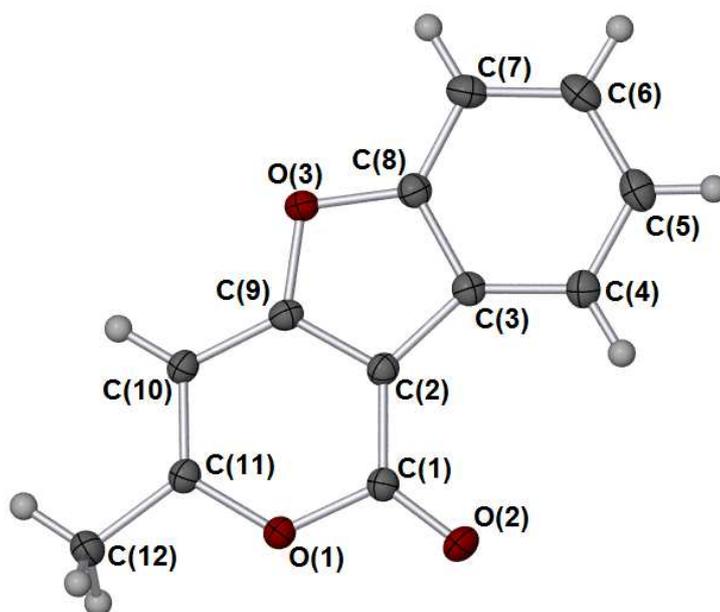
**Details of Crystallographic Analysis** Diffraction data were collected at 110 K on a Bruker Smart Apex diffractometer with Mo-K $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ) using a SMART CCD camera. Diffractometer control, data collection and initial unit cell determination was performed using “SMART”.<sup>[7]</sup> Frame integration and unit-cell refinement software was carried out with “SAINT+”.<sup>[8]</sup> Absorption corrections were applied by SADABS (v2.10, Sheldrick). Structures were solved by direct methods using SHELXS-97<sup>[9]</sup> and refined by full-matrix least squares using SHELXL-97.<sup>[9]</sup> All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed using a “riding model” and included in the refinement at calculated positions.

The anion of IJF1002m (**12**) was modelled as a 98:2 disordered mixture of PF $_6^-$  and  $\Gamma$  respectively.

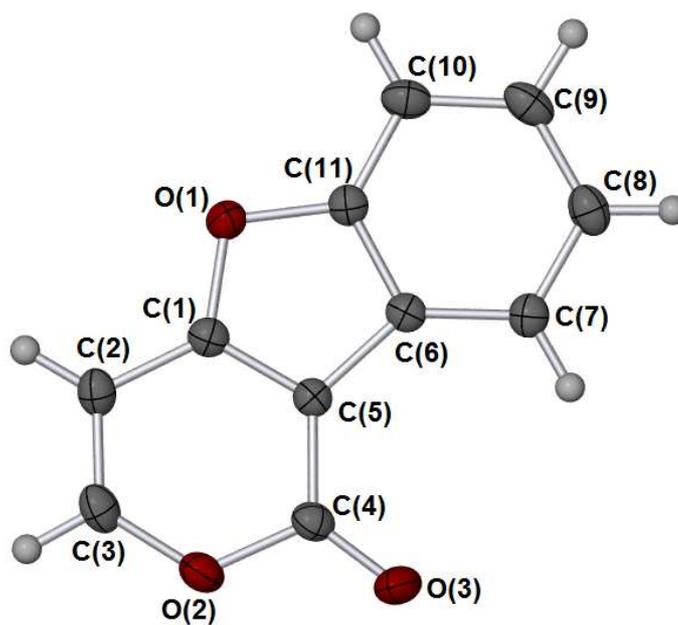
**Table:** X-ray diffraction details for all compounds.

Compound reference	ijf0925m ( <b>6a</b> )	ijf0934m ( <b>6b</b> )	ijf0930 ( <b>8h</b> )	ijf0931 ( <b>8i</b> )	ijf0936m ( <b>10</b> )	ijf1002m ( <b>12</b> )
Chemical formula	C <sub>12</sub> H <sub>8</sub> O <sub>3</sub>	C <sub>11</sub> H <sub>6</sub> O <sub>3</sub>	C <sub>12</sub> H <sub>7</sub> FO <sub>3</sub>	C <sub>12</sub> H <sub>7</sub> FO <sub>3</sub>	C <sub>48</sub> H <sub>39</sub> IO <sub>3</sub> P <sub>2</sub> Pd	C <sub>30</sub> H <sub>24</sub> O <sub>3</sub> P•(F <sub>6</sub> P <sub>1</sub> ) <sub>0.98</sub> •(I) <sub>0.02</sub>
Formula Mass	200.18	186.16	218.18	218.18	959.03	608.43
Crystal system	Triclinic	Monoclinic	Triclinic	Triclinic	Monoclinic	Triclinic
<i>a</i> /Å	7.1467(5)	11.1190(16)	3.7437(3)	3.7597(2)	10.2109(5)	7.8107(8)
<i>b</i> /Å	7.3546(5)	8.2091(12)	6.3700(7)	6.1644(4)	11.8937(6)	13.2530(14)
<i>c</i> /Å	9.3252(6)	18.856(3)	19.0219(19)	19.6660(11)	34.1332(17)	14.2579(15)
<i>α</i> /°	69.7600(10)	90.00	91.665(9)	92.543(5)	90.00	97.040(2)
<i>β</i> /°	81.8920(10)	105.787(2)	90.858(7)	90.715(5)	93.0340(10)	104.389(2)
<i>γ</i> /°	75.2200(10)	90.00	93.699(8)	90.125(5)	90.00	104.932(2)
Unit cell volume/Å <sup>3</sup>	443.91(5)	1656.2(4)	452.42(8)	455.30(5)	4139.5(4)	1353.6(2)
Temperature/K	120(2)	110(2)	120(2)	120(2)	110(2)	110(2)
Space group	<i>P</i> 1	<i>C</i> 2/ <i>c</i>	<i>P</i> 1	<i>P</i> 1	<i>P</i> 2(1)/ <i>n</i>	<i>P</i> 1
No. of formula units per unit cell, <i>Z</i>	2	8	2	2	4	2
No. of reflections measured	6084	8041	7806	4447	55989	13874
No. of independent reflections	2211	2057	1688	1706	10290	6661
<i>R</i> <sub>int</sub>	0.0124	0.0175	0.0390	0.0286	0.0494	0.0235
Final <i>R</i> <sub><i>I</i></sub> values ( <i>I</i> > 2σ( <i>I</i> ))	0.0352	0.0373	0.0480	0.0477	0.0330	0.0490
Final <i>wR</i> ( <i>F</i> <sup>2</sup> ) values ( <i>I</i> > 2σ( <i>I</i> ))	0.1005	0.0970	0.1249	0.1335	0.0684	0.1227
Final <i>R</i> <sub><i>j</i></sub> values (all data)	0.0366	0.0443	0.0574	0.0514	0.0456	0.0719
Final <i>wR</i> ( <i>F</i> <sup>2</sup> ) values (all data)	0.1023	0.1024	0.1316	0.1382	0.0730	0.1367
CCDC number	764708	764709	773153	773154	764710	764711

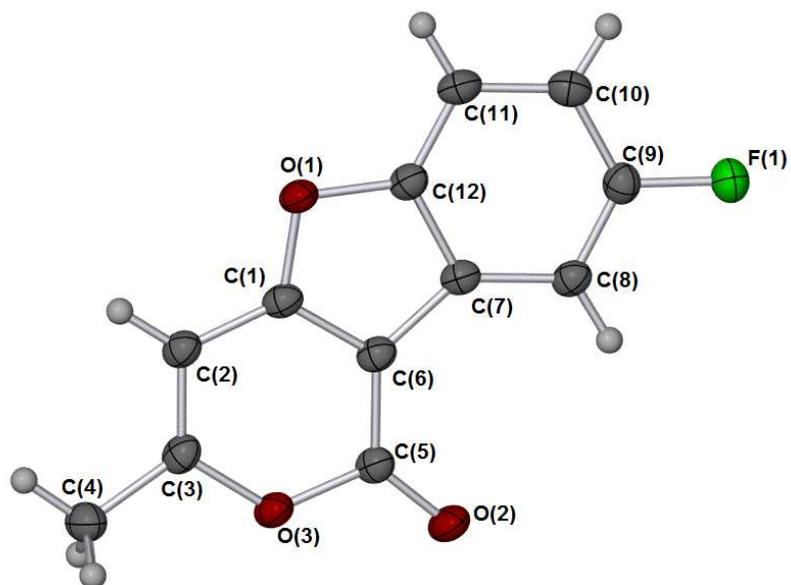
X-ray structure of **6a** (ijf0925m)



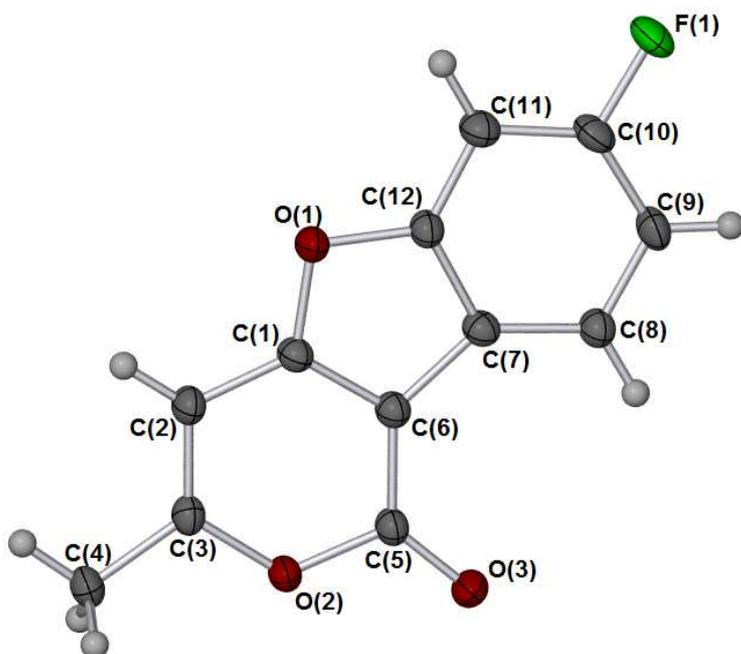
X-ray structure for **6b** (ijf0934m)

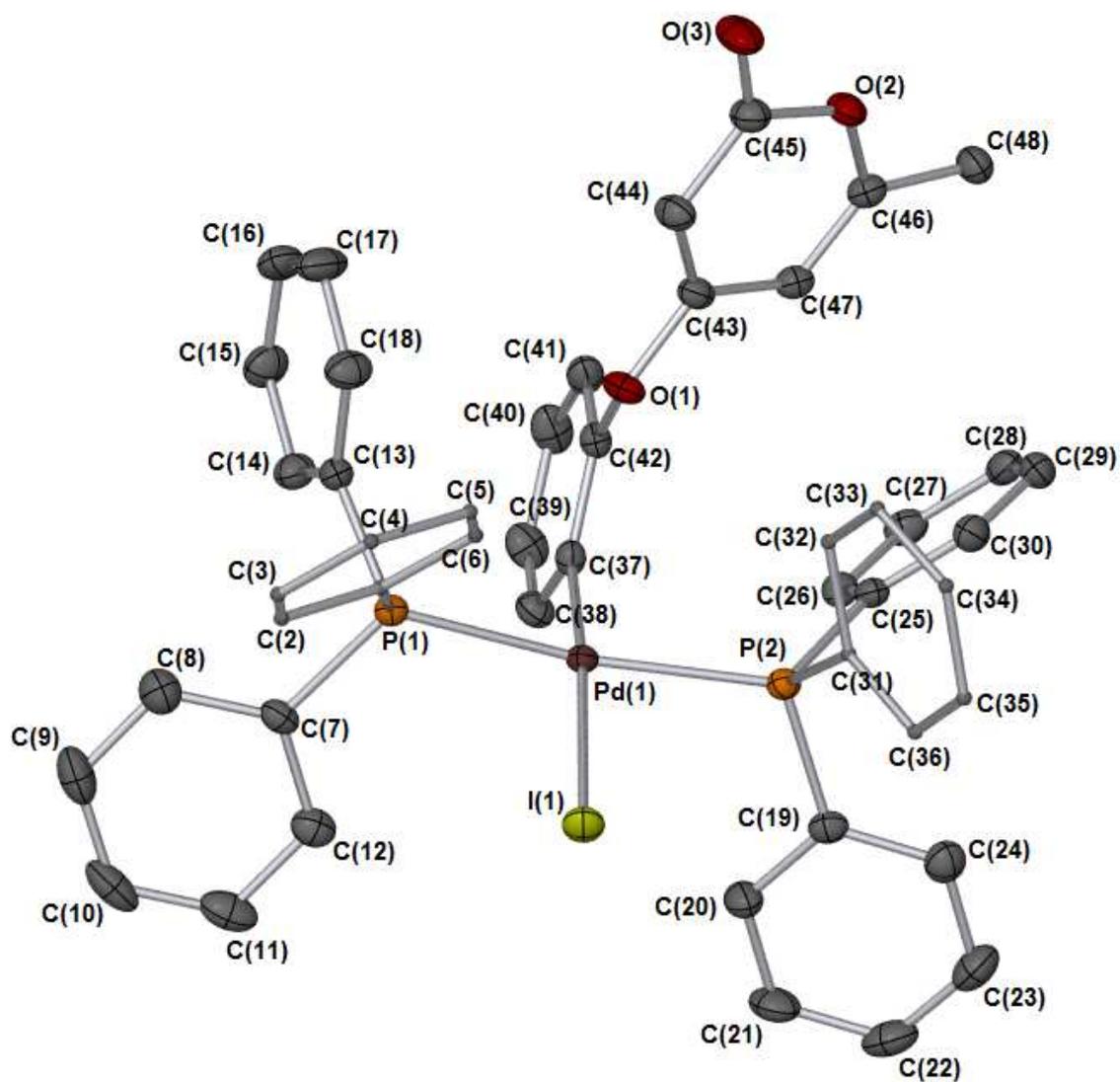


X-ray structure for **8h** (ijf0930m)

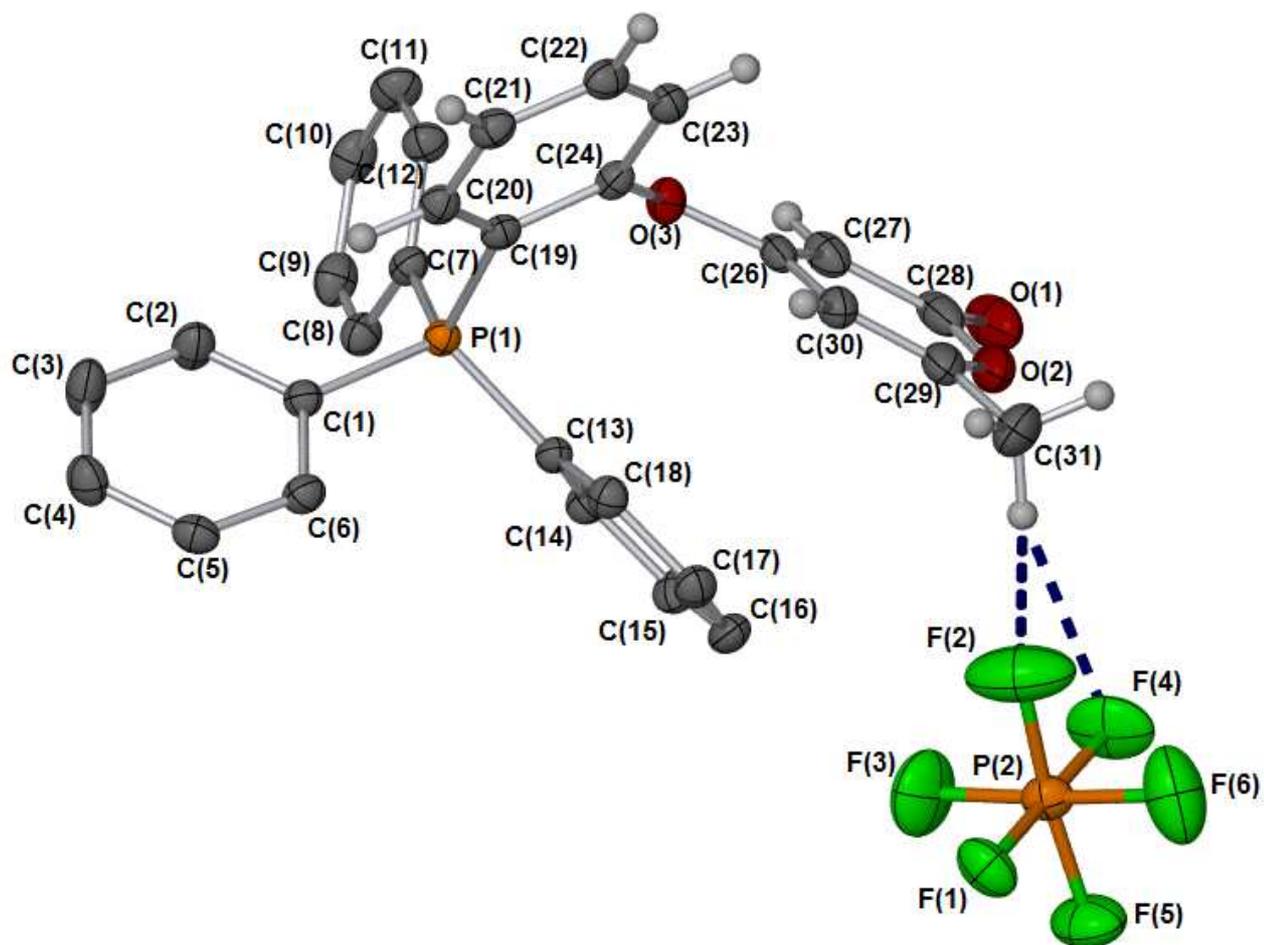


X-ray structure for **8i** (ijf0931m)





X-ray structure of the phosphonium salt (12) (ijf1002m)



## 5. References

---

- [1] Y. Kato, S. Okada, K. Tomimoto and T. Mase, *Tetrahedron Lett.*, 2001, **42**, 4849.
- [2] K. Afarinkia, M. J. Bearpark and A. Ndibwami, *J. Org. Chem.*, 2003, **68**, 7158.
- [3] R. F. Clark, T. Zhang, X. Wang, R. Wang, X. Zhang, H. S. Camp, B. A. Beutal, H. L. Sham and Y. G. Gu, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 1961.
- [4] X. Zhang, M. McLaughlin, R. Lizeth, P. Munoz, R. P. Hsung, J. Wang and J. Swidorski, *Synthesis*, 2007, **5**, 749.
- [5] A. Spaggiari, D. Vaccari, P. Davoli, G. Torre and F. Prati, *J. Org. Chem.*, 2007, **72**, 2216.
- [6] M. E. Jung and D. A. Allen, *Org. Lett.*, 2009, **11**, 757.
- [7] *Smart diffractometer control software (v5.625)*, Bruker-AXS, Bruker AXS GmbH, Karlsruhe, Germany.
- [8] *Saint+ (v6.22)* Bruker AXS, Bruker AXS GmbH, Karlsruhe, Germany.
- [9] G. M. Sheldrick, *SHELXS-97, Program for the Solution of Crystal Structures*, Universität Göttingen, **1997**.